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REGULATION OF CEREBRAL CARBON DIOXIDE

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Students of cerebral function have, in general, paid too little attention to carbon dioxide. Procedures which alter the tension of carbon dioxide in the brain have a pronounced effect on cerebral function [1] and on the electrical activity of the cortex.[2] As shown by some of these experiments, extreme shifts in the carbon dioxide tension of the brain are

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1. Rosett, J.: The Experimental Production of Rigidity, of Abnormal Involuntary Movements and of Abnormal States of Consciousness in Man, Brain **47**:293-336, 1924. Foerster, O.: Hyperventilationsepilepsie, Deutsche Ztschr. f. Nervenh. **83**:347-356, 1924-1925. Lennox, W. G., and Cobb, S.: The Relation of Certain Physicochemical Processes to Epileptiform Seizures, Am. J. Psychiat. **8**:837-847, 1929. Loevenhart, A. S.; Lorenz, W. F., and Waters, R. M.: Cerebral Stimulation, J. A. M. A. **92**:880-883 (March 16) 1929. d'Elseaux, F. C., and Solomon, H. C.: Use of Carbon Dioxide Mixtures in Stupors Occurring in Psychoses, Arch. Neurol. & Psychiat. **29**:213-230 (Feb.) 1933. Gellhorn, E., and Kraines, S. H.: Word Associations as Affected by Deficient Oxygen, Excess of Carbon Dioxide and Hyperpnea, ibid. **38**:491-504 (Sept.) 1937.

2. (*a*) Gibbs, F. A.; Davis, H., and Lennox, W. G.: The Electro-Encephalogram in Epilepsy and in Conditions of Impaired Consciousness, Arch. Neurol. & Psychiat. **34**:1133-1148 (Dec.) 1935. (*b*) Lennox, W. G.; Gibbs, F. A., and Gibbs, E. L.: Effect on the Electro-Encephalogram of Drugs and Conditions Which Influence Seizures, ibid. **36**:1236-1245 (Dec.) 1936; (*c*) Relationship in Man of Cerebral Activity to Blood Flow and to Blood Constituents, J. Neurol. & Psychiat. **1**:211-225, 1938. (*d*) Gibbs, F. A.; Williams, D., and Gibbs, E. L.: Modification of the Cortical Frequency Spectrum by Changes in CO_2, Blood Sugar and O_2, J. Neurophysiol. **3**:49-58, 1940.

disadvantageous. Therefore, a mechanism which would provide for the homeostasis of carbon dioxide would be advantageous. Such a mechanism appears to reside in the response of cerebral blood vessels to changes in alveolar or arterial carbon dioxide.

An increase of carbon dioxide tension in the cerebral blood vessels causes dilatation of the cerebral arterioles, and a decrease causes constriction. In contrast, a maximal increase of oxygen tension produces only feeble constriction, and an extreme decrease in oxygen tension causes only moderate dilatation. These facts have been abundantly proved both for animals [3] and for man [4] by workers employing a variety of technics.

Dilatation of arterioles with high carbon dioxide tension and constriction with low carbon dioxide tension is more or less peculiar to the brain; arterioles of the arm and leg dilate with low carbon dioxide tension and constrict with high carbon dioxide tension.[4b] The dilatation of the vascular bed in the arms and legs with low carbon dioxide tension tends to wash carbon dioxide out of the arms and legs, thus maintaining the carbon dioxide level of the general circulation to the advantage of the brain but to the disadvantage of the arms and legs. The constrictor response of the cerebral blood vessels to a falling arterial carbon dioxide tension aids the brain directly because the escape of carbon dioxide from the brain is thereby prevented. In order to test the competence of the mechanism for maintaining a nearly constant cerebral carbon dioxide level, the following experiments were carried out.

EXPERIMENTAL PROCEDURE

The subjects used were 7 healthy medical students whose resting brain waves were normal and 6 hospital patients with normal brain waves and no evidence of disease of the brain. Each subject was placed in the prone position. His electroencephalograph was recorded, and from inlying needles in the internal jugular vein and the femoral artery simultaneous samples of blood were drawn before, during and after a period in which the carbon dioxide level of arterial blood was altered. In 13

3. Wolff, H. G., and Lennox, W. G.: The Effect on Pial Vessels of Variations in the Oxygen and Carbon Dioxide Content of the Blood, Arch. Neurol. & Psychiat. **23**:1097-1120 (June) 1930. Schmidt, C. F.: The Intrinsic Regulation of the Circulation in the Parietal Cortex of the Cat, Am. J. Physiol. **114**:572-585, 1936.

4. (*a*) Cobb, S., and Fremont-Smith, F.: Changes in the Human Retinal Circulation and in the Pressure of the Cerebrospinal Fluid During Inhalation of a Mixture of Carbon Dioxide and Oxygen, Arch. Neurol. & Psychiat. **26**:731-736 (Oct.) 1931. (*b*) Lennox, W. G., and Gibbs, E. L.: The Blood Flow in the Brain and the Leg of Man, and the Changes Induced by Alteration of Blood Gases, J. Clin. Investigation **11**:1155-1177, 1932. (*c*) Ferris, E. B., Jr.: Objective Measurement of Relative Intracranial Blood Flow in Man, with Observations Concerning the Hydrodynamics of the Craniovertebral System, Arch. Neurol. & Psychiat. **46**:377-401 (Sept.) 1941.

experiments the subjects overventilated their lungs for two or three minutes; in 4 they breathed room air to which carbon dioxide was added in increasing concentrations. The oxygen and carbon dioxide contents and the p_H of the blood samples were measured, and the oxygen saturations and carbon dioxide tensions were calculated. Under the conditions of these experiments an increased arteriovenous difference in oxygen content was considered indicative of a diminished cerebral blood flow and cerebral vasoconstriction and a decreased arteriovenous difference in oxygen content indicative of cerebral vasodilatation and accelerated flow. Studies with a thermoelectric flow recorder [5] have shown that these are valid assumptions for the present experimental conditions. The degree of overventilation was judged not by the volume of respired air but by the drop in the carbon dioxide content of the arterial blood.

RESULTS

A given amount of overventilation may or may not result in pronounced slowing of brain waves. The subjects were divided into two groups on the basis of whether or not slowing of their cortical waves occurred. The first 11 subjects chosen at random showed no definite slowing despite overventilation which was sufficient to produce a great decrease in the arterial carbon dioxide. Since we wished to make comparative observations on persons whose cortical rhythms were easily slowed by overventilation, 6 additional subjects were tested. Of these, 2 showed slowing with overventilation and were added to the original 11 subjects to make up the group of the 13 who overventilated their lungs while samples of blood were being taken.

The results in a typical experiment with a subject whose brain waves were not slowed are presented in figure 1 and table 1. Inspection of this figure reveals that the overventilation was accompanied by a sharp drop in carbon dioxide content and tension and an increase in the p_H of arterial blood (p_H scale reversed). In contrast, there was little decrease in the carbon dioxide content of internal jugular venous blood. The carbon dioxide tension decreased more than the carbon dioxide content, largely because of the drop in oxygen saturation. Reduced hemoglobin is more alkaline than oxyhemoglobin. The question whether for the present experiments carbon dioxide content or carbon dioxide tension in the internal jugular vein is a better indicator of the carbon dioxide pressure in the electrically active cortex will not be discussed at this time. Blood from the internal jugular vein is admittedly not a direct indicator of conditions in the brain, but recent experimental work by Courtice [6] indicates that the carbon dioxide tension in the brain and in the internal jugular venous blood are very nearly the same. Production rates, gradients and storage capacities will have to be taken into account in a

5. Gibbs, F. A.; Gibbs, E. L., and Lennox, W. G.: Changes in Human Cerebral Blood Flow Consequent on Alterations in Blood Gases, Am. J. Physiol. **111**:557-563, 1935.

6. Courtice, F. C.: The Gaseous Tensions in the Brain, J. Physiol. **100**:192-197, 1941.

final statement of the changes that occur with alterations in any given factor, but either carbon dioxide content or carbon dioxide tension in the internal jugular venous blood is satisfactory for describing the fundamental mechanism involved in these experiments.

The concentration of carbon dioxide was abnormal in blood entering the brain but nearly normal in blood leaving it, and the electrical activity of the cortex remained almost unchanged. This was achieved by means

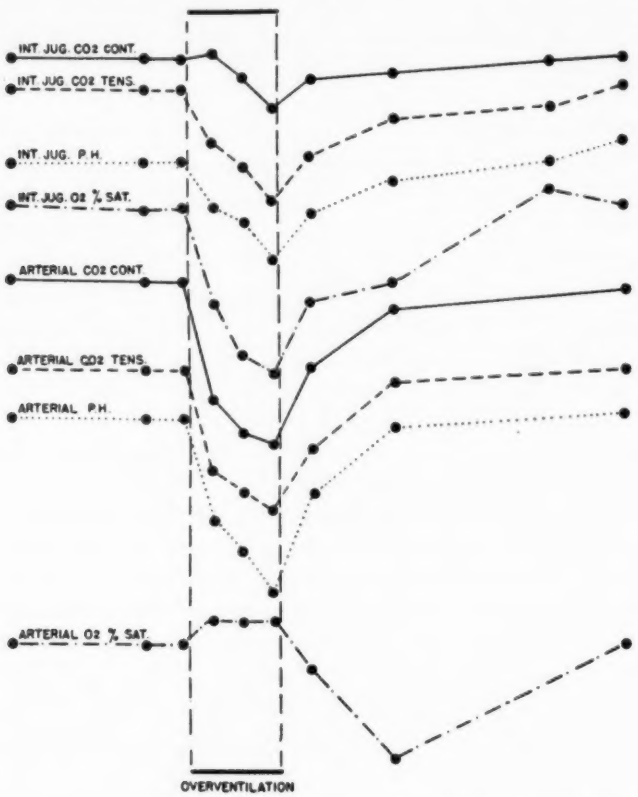

Fig. 1.—Effect of overventilation on the p_H (scale reversed), the blood gases and the cerebral blood flow of healthy subject Zo. The brain waves of this subject were not slowed appreciably by the hyperpnea. Six minutes of overventilation is indicated by the horizontal heavy line. The actual values from which these curves were plotted are given in table 1.

of a constriction of cerebral arterioles, as shown by a sharply decreased oxygen saturation of internal jugular venous blood (and an increased arteriovenous difference in oxygen content). These changes resulted in cerebral hypoxemia, but they succeeded in maintaining the carbon dioxide level in the brain (judged by the values for internal jugular venous blood) at a relatively normal level. In other words, within the limits

set by these experiments there was homeostasis for the cerebral carbon dioxide level and none for oxygen.

The alterations in the oxygen saturation of internal jugular venous blood which appear in figure 1 are explained by the changes in blood flow which accompany the change in caliber of the cerebral vessels. In this and in similar experiments on subjects with cerebral blood vessels which respond normally to carbon dioxide, changes in the oxygen content of internal jugular venous blood are secondary to changes in the carbon dioxide content of arterial blood; i. e., venous oxygen is a function of arterial carbon dioxide. This relation holds because of the fact that when the arterial carbon dioxide falls and the cerebral vessels constrict, the flow of blood through the brain is diminished and more oxygen is

TABLE 1.—*Effect of Overventilation on the p_H, the Blood Gases and the Cerebral Blood Flow of Healthy Subject Zo, Whose Brain Waves Were Not Slowed*

	Internal Jugular Venous Blood				Arterial Blood			
	Carbon Dioxide, Vol. %		Oxygen, Percentage Saturation		Carbon Dioxide, Vol. %		Oxygen, Percentage Saturation	
Relation to Overventilation	Content	Tension		p_H	Content	Tension		p_H
Before 1	53.1	47.2	58.6	7.375	46.6	36.6	93.6	7.440
2	53.2	47.3	57.6	7.375	46.4	36.7	93.1	7.438
3	53.1	47.2	58.6	7.374	46.6	36.6	93.6	7.440
During 1	53.5	40.0	45.8	7.454	38.7	23.3	96.1	7.572
2	51.8	36.9	39.1	7.474	36.6	20.3	95.6	7.611
3	49.5	32.1	36.5	7.524	35.8	17.7	96.1	7.667
After 1	51.7	38.1	45.8	7.464	40.8	26.3	90.0	7.535
2	51.9	42.8	48.4	7.409	44.8	34.7	78.1	7.444
3	52.8	45.2	60.7	7.393	.....	.....	.....	.....
4	53.1	48.3	58.6	7.363	46.1	37.4	93.1	7.425

removed from each cubic centimeter of blood that flows through. Thus, as the arterial carbon dioxide falls, the internal jugular venous oxygen will fall also. Conversely, with a dilatation of cerebral vessels produced by a high concentration of carbon dioxide, the oxygen tension of the internal jugular venous blood will rise as the carbon dioxide tension of arterial blood rises. Under such conditions, since the arterial oxygen is essentially constant, internal jugular venous oxygen is an indicator of cerebral blood flow. Measurement of the carbon dioxide content of the internal jugular venous blood gives the other side of the picture; as the arterial carbon dioxide falls and the cerebral vessels constrict, the cerebral blood flow decreases and more carbon dioxide has to be carried by each cubic centimeter of blood; thus the carbon dioxide content of the internal jugular venous blood rises, and the rise is ordinarily almost enough to compensate for the decline in arterial carbon dioxide.

The next experiments were performed on 2 subjects, chosen because a short period of overventilation had resulted in pronounced slowing of

brain waves. In these 2 subjects it was found that overventilation resulted in practically the same drop in arterial carbon dioxide content (and tension) as had occurred in the preceding group, in which there had been no slowing of the brain waves. However, these 2 subjects differed from the others in this respect—the carbon dioxide in the

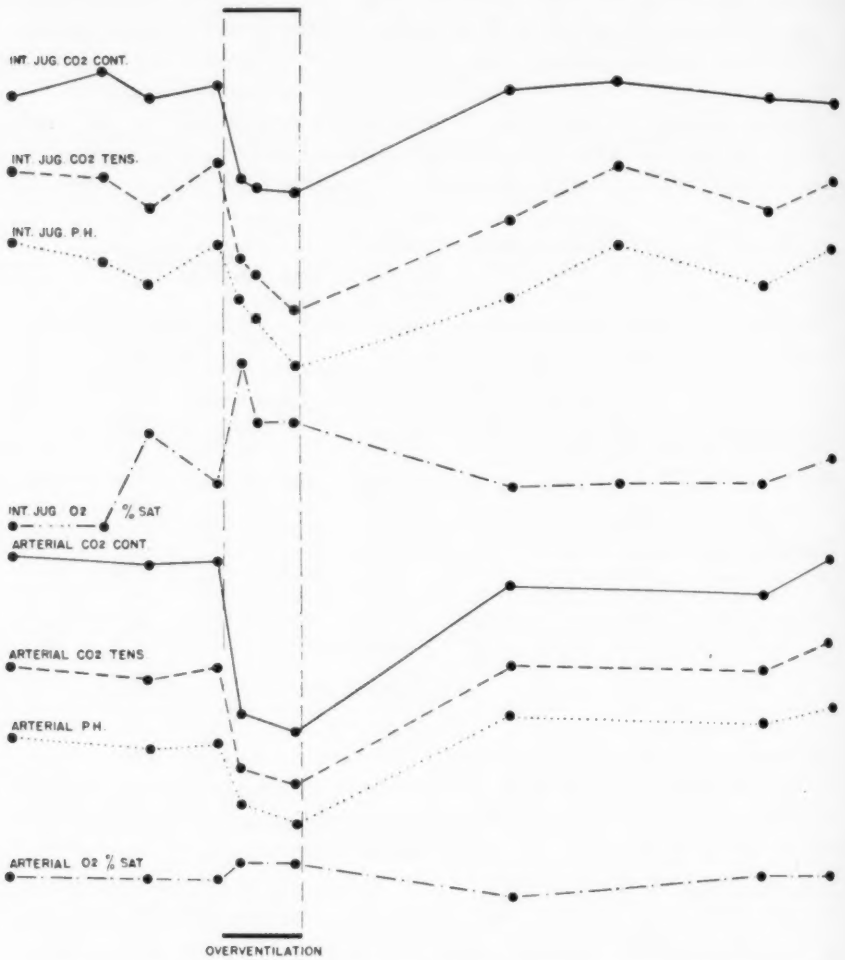

Fig. 2.—Effect of overventilation on the p_H (scale reversed), the blood gases and the cerebral blood flow of healthy subject Fr. Slow, high voltage brain waves occurred during the hyperpnea. Five minutes of overventilation is indicated by the horizontal heavy line. The actual values from which these curves were plotted are given in table 2.

internal jugular venous blood decreased greatly (fig. 2 and table 2). The drop in the carbon dioxide of the internal jugular venous blood occurred because the cerebral arterioles dilated instead of constricting, as

was shown by a rise in the oxygen saturation of internal jugular venous blood. It is, therefore, the decrease in cerebral carbon dioxide tension, as indicated by the carbon dioxide content and tension of internal jugular venous blood, which correlates with the slowing of the brain waves.

Davis and Wallace [7] expressed the belief that in their experiments with overventilation the slowing of the brain waves was due to extreme cerebral vasoconstriction and resulting anoxia. Their study was based on analysis of blood from the finger tip. Even if such blood were purely arterial, which it is not, it would be adequate only for determining the extent to which the overventilation had been successful in reducing the arterial carbon dioxide level, and this, as we have pointed out, is by no

TABLE 2.—*Effect of Overventilation on the p_H, the Blood Gases and the Cerebral Blood Flow of Healthy Subject Fr, Whose Brain Waves Were Slowed*

	Internal Jugular Venous Blood				Arterial Blood			
	Carbon Dioxide, Vol. %		Oxygen, Percentage Saturation		Carbon Dioxide, Vol. %		Oxygen, Percentage Saturation	
Relation to Overventilation	Content	Tension		p_H	Content	Tension		p_H
Before 1	50.1	51.0	59.5	7.310	45.3	38.9	93.9	7.402
2	51.8	50.3	60.0	7.334	.....	.....	.....	.....
3	50.0	45.7	72.6	7.365	44.7	37.1	94.3	7.418
4	50.9	52.0	65.5	7.309	45.3	38.9	93.9	7.403
During 1	44.6	39.2	81.7	7.385	34.8	24.9	96.8	7.491
2	44.1	36.9	73.1	7.410	.....	.....	.....	.....
3	43.6	32.1	73.6	7.472	33.4	23.9	97.3	7.502
After 1	50.2	44.3	64.5	7.381	43.4	39.3	91.9	7.376
2	50.7	51.4	65.0	7.313	.....	.....	.....	.....
3	49.6	45.2	64.5	7.365	42.4	38.8	94.8	7.378
4	49.5	49.7	68.5	7.318	45.3	41.6	94.8	7.369

means a crucial determinant of cortical frequency. Our measurements on the gases of the blood entering and leaving the brain showed that those subjects who reacted to overventilation by slowing had little or no reduction of oxygen content of the internal jugular venous blood and feeble, or no, cerebral vasoconstriction. On the other hand, all subjects who showed no slowing had marked constriction and a definite fall in internal jugular venous oxygen. If the constrictor mechanism is grossly defective—for example, if the cerebral arterioles dilate when the carbon dioxide in arterial blood is reduced—the carbon dioxide of blood in the internal jugular vein (and in the brain) will fall to an exceedingly low level (fig. 2). Such a defective response is common in patients with

7. Davis, H., and Wallace W. McL.: Electroencephalographic and Subjective Changes Produced by Standardized Hyperventilation, Arch. Neurol. & Psychiat., to be published.

petit mal epilepsy and is associated with a great decrease in the frequency and an increase in amplitude of the electrical waves from the cortex.[8]

The contrasting effect of overventilation in the two types of subjects is shown in simplified form in figure 3. The subject, values for whom are shown at the left had no change in the carbon dioxide of the internal jugular venous blood or in the brain waves because he had marked cerebral constriction, as evidenced by the fall in oxygen in the internal

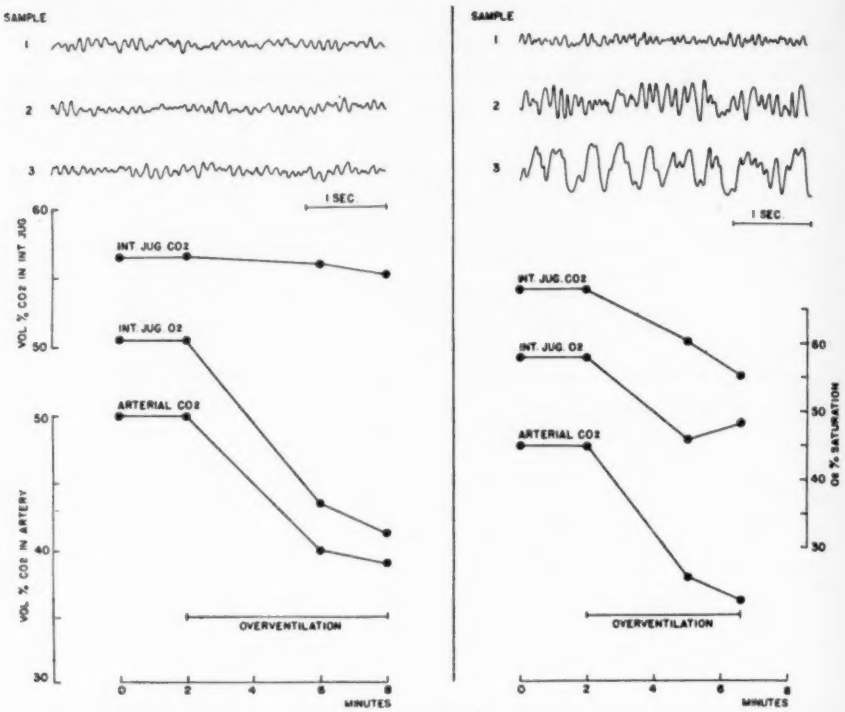

Fig. 3.—Comparative effect of overventilation on the brain waves and on the cerebral blood flow of subject Pa (left hand panel) and subject Ri (right hand panel). The three tracings at the top were taken, respectively, before, during and at the close of overventilation, the duration of which is indicated by the horizontal line at the bottom of the chart. On the left, the scales give the carbon dioxide content of internal jugular venous and of arterial blood in terms of volumes per cent. On the right, the scale indicates the percentage oxygen saturation of internal jugular venous blood. In the subject data for whom appear on the left overventilation caused no change in brain waves and a greatly decreased cerebral blood flow, with maintenance of a stable carbon dioxide tension. In the subject data for whom appear on the right overventilation caused slow, high voltage waves, the result of a relatively small decrease in cerebral blood flow and lowered carbon dioxide tension of internal jugular venous blood.

8. Nims, L. F.; Gibbs, E. L.; Lennox, W. G.; Gibbs, F. A., and Williams, D.: Adjustment of Acid-Base Balance of Patients with Petit Mal to Overventilation, Arch. Neurol. & Psychiat. **43**:262-269 (Feb.) 1940.

jugular venous blood. In the experiment represented at the right, overventilation produced successive slowing of brain waves, until the frequency was only 3 per second. The carbon dioxide content of internal jugular venous blood fell because cerebral vasoconstriction was only moderate and was not maintained until the period of hyperpnea was over.

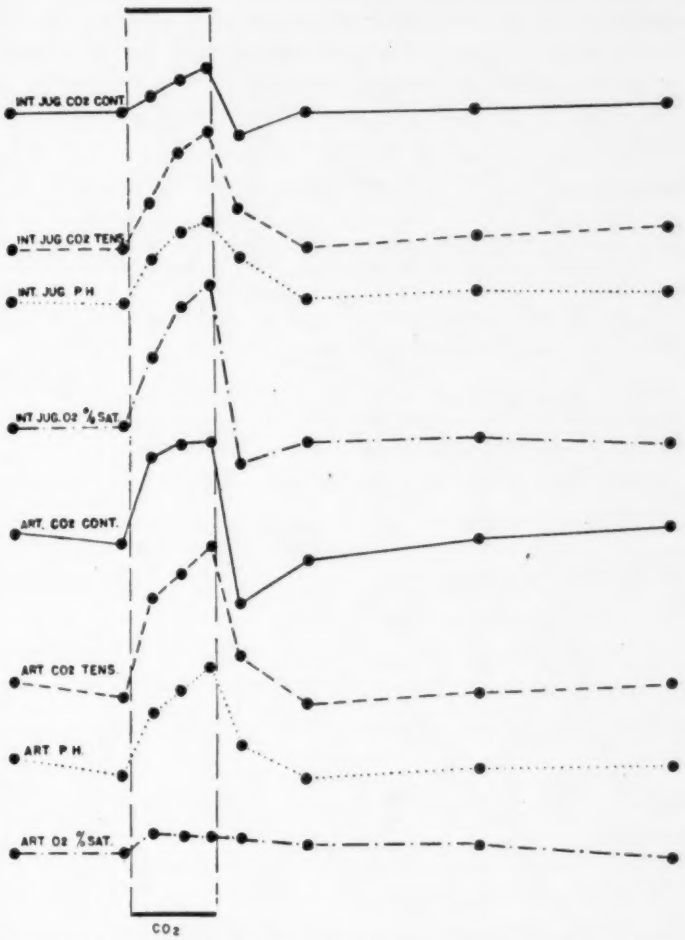

Fig. 4.—Effect of breathing an increased concentration of carbon dioxide in air on the p_H (scale reversed), the blood gases and the cerebral circulation of subject Va. Carbon dioxide was introduced into the air breathed in increasing proportions until the maximum hyperpnea which the subject could tolerate was reached, after six and a half minutes. The actual values from which these curves were plotted are given in table 3.

There are all degrees of competence of this cerebral vasoconstrictor mechanism in supposedly normal adults. The most commonly encoun-

tered defect is the inability, just mentioned, to maintain a steady cerebral carbon dioxide tension by gradually relaxing the constriction in the post-overventilation period. Very often the constriction is abandoned as soon as the arterial carbon dioxide starts to rise, with the result that the carbon dioxide in the blood of the internal jugular vein (and in the brain) falls lower after than it did during the period of overventilation.

Overventilation, if sufficiently prolonged, will produce slow waves in the electroencephalograms of most normal persons, for the constriction, when it occurs, cannot compensate indefinitely for a decline in arterial carbon dioxide. The cerebral vessels abandon their constriction before the cerebral oxygen supply is reduced to the critical point at which the slow waves appear from oxygen lack; i. e., the constriction is abandoned

TABLE 3.—*Effect of Breathing Increased Concentrations of Carbon Dioxide on the p_H, the Blood Gases and the Cerebral Blood Flow of Healthy Subject Va*

	Internal Jugular Venous Blood				Arterial Blood			
	Carbon Dioxide, Vol. %		Oxygen, Percentage Saturation		Carbon Dioxide, Vol. %		Oxygen, Percentage Saturation	
Relation to Overventilation	Content	Tension		p_H	Content	Tension		p_H
Before 1	55.6	49.4	67.2	7.393	50.0	42.1	93.1	7.425
2	55.3	49.0	66.9	7.397	49.1	39.2	93.1	7.451
During 1	56.4	54.9	76.3	7.349	55.0	52.7	95.4	7.360
2	57.7	61.6	82.8	7.305	55.7	55.7	94.8	7.337
3	58.4	64.0	86.0	7.292	55.8	59.9	95.0	7.305
After 1	53.8	53.6	61.0	7.332	45.3	45.2	94.8	7.337
2	55.2	48.6	64.5	7.394	48.1	38.7	93.9	7.447
3	55.4	49.9	65.6	7.384	49.4	40.2	93.9	7.440
4	55.8	50.1	64.5	7.386	50.5	41.4	92.0	7.436

when the oxygen saturation of the blood in the internal jugular vein falls to approximately 30 per cent.[2c] Thus, if a subject overventilates while breathing a 4 per cent oxygen mixture, no constriction of cerebral vessels occurs.

Davis and Wallace [7] reported that raising the sugar and oxygen levels of arterial blood helps to prevent the slowing which occurs with overventilation. This, we believe, may be explained as follows: The cerebral vessels constrict only to the point where vital supplies of energy to the brain are threatened. If the concentrations of sugar and oxygen in the arterial blood are raised, the cerebral blood vessels will be able to constrict further, and therefore their ability to compensate for a fall in arterial carbon dioxide will be enhanced.

Experiments were conducted in which the carbon dioxide content of arterial blood was increased. An example of the response of a normal healthy adult to breathing an increasing concentration of carbon dioxide is shown in figure 4 and table 3. It is evident that the increased arterial

carbon dioxide causes dilatation of cerebral arterioles and increased cerebral blood flow, which succeeds to a remarkable degree in maintaining the carbon dioxide content of the internal jugular venous blood, and therefore the cerebral carbon dioxide tension, at or near the preceding level. No subject or patient has been found in whom this dilator response to high carbon dioxide concentration was grossly defective.

SUMMARY AND CONCLUSIONS

The response to overventilation and to breathing an increased concentration of carbon dioxide was studied in 13 subjects with normal electroencephalograms and no clinical evidence of cerebral disorder. Two of the subjects were chosen because they showed an unusually rapid increase in amplitude and decrease in frequency of cortical potentials with overventilation. Simultaneous samples of blood were taken from the femoral artery and the internal jugular vein, and the values obtained for carbon dioxide content, p_H, carbon dioxide tension and oxygen saturation were compared and correlated with simultaneously obtained samples of the electroencephalogram.

1. The dilatation or constriction of cerebral arterioles which follows an increase or decrease of carbon dioxide in the arterial blood serves to protect the brain against undue shifts in carbon dioxide tension.

2. The slow waves that appear in the electroencephalogram with overventilation are caused by a drop in cerebral carbon dioxide, and not by anoxia secondary to cerebral vasoconstriction.

3. The ease with which such slow waves can be produced with overventilation is a rough index of the relative incompetence of the cerebral vasoconstrictor response to low carbon dioxide tension.

4. In some supposedly healthy adults and in most persons with petit mal epilepsy, the cerebral vasoconstrictor response to low carbon dioxide tension is defective, this defect resulting in abnormal slowing of the electrical activity of the cortex during overventilation.

5. The cerebral vasoconstrictor response to low carbon dioxide tension disappears when a critically low level of oxygen tension is reached.

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EPIDERMOID, DERMOID AND TERATOMATOUS TUMORS OF THE CENTRAL NERVOUS SYSTEM

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The epidermoid, dermoid and teratoma are essentially similar tumors both in their development and in their clinical course. They belong to the tumors of mixed tissue which arise from cell rests. The type of tumor depends on the embryonic derivation of its elements. When the neoplasm contains tissues from all three germ layers it is considered a true teratoma. When tissues of mesodermal as well as epithelial origin are represented, it is called a dermoid cyst. The most common and simplest type, the epidermoid, is composed of elements of but one germ layer, the ectoderm. Sections from different areas in the wall of a single tumor have occasionally shown dermoid in one part and epidermoid in another.[1] These mixed tumors, comprising a rare but interesting group of neoplasms of the central nervous system, are discussed under the following subdivisions, and 14 cases observed are reported.

	No. of Cases
A. Epidermoid	
1. Intracranial	6
2. Intradiploic	2
3. Of the spinal canal	1
B. Dermoid	
1. Intracranial	1
2. Of the spinal canal	0
C. Teratoma	
1. Intracranial	2
2. Of the spinal canal	2

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1. Montgomery, G. L., and Finlayson, D. I. C.: Cholesteatoma of the Middle and Posterior Cranial Fossae, Brain **57**:177, 1934.

INTRACRANIAL EPIDERMOID, OR CHOLESTEATOMA

Frequency.—Tooth [2] found 1 epidermoid in 258 verified brain tumors, Bernhardt [3] 1 in 487, Alpers [4] 8 in 758 and Mahoney [5] 15 in 2,500. When Bailey,[6] in 1920, reported the first successful operative removal of an intracranial epidermoid, 62 such tumors had been reported in the literature.

Structure.—Grossly the epidermoid is sharply circumscribed and nodular, with a smooth, glistening external sheen, which becomes dull when the tumor is exposed to the air or placed in a fixative. The growth is avascular; no blood vessels pass into it. It has a definite fibrous capsule, the outer surface of which is sometimes covered by a dense layer of calcium. The interior contains a grayish or whitish, soft, necrotic, caseous-like material, which not uncommonly has a lamellar arrangement and a waxy consistency. The size is extremely variable, the larger tumors replacing large areas of brain tissue.

Histologically, the capsule wall is composed of definite layers, which Bailey [6] designated by special names. The outermost layer consists of thick bundles of fibers and is called the stratum durum. Next occurs a layer of stratified epithelium, the stratum granulosum. This layer resembles the stratified epithelium of the epidermis, its outermost cells being large and polygonal while its innermost cells are small and somewhat columnar and contain many deeply stained granules, called keratohyaline granules. Bailey [6] also mentioned a stratum fibrosum and a stratum cellulosum, but in most cases the tissues beneath the granular layer merge with the central mass of the epidermoid. The interior of the tumor is composed of long, structureless fibers and broken-down debris, consisting of cholesterol crystals and fatty material and in some tumors masses of flattened, structureless cells, called "woody cells." Histologically, therefore, the epidermoid is primarily an epithelial tumor, the mesodermal elements being only supporting.

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2. Tooth, H.: The Treatment of Tumors of the Brain: The Indications for Operation, Tr. Internat. Cong. Med., London, sect. 11, Neuropath., 1913, p. 161.

3. Bernhardt, M.: Ueber einen in der Dürener Irrenanstalt beobachteten Fall von Cholesteatom, Allg. Ztschr. f. Psychiat. **46**:30, 1890.

4. Alpers, B.: The Cerebral Epidermoids (Cholesteatomas), Am. J. Surg. **43**:55, 1939.

5. Mahoney, W.: Die Epidermoide des Zentralnervensystems Ztschr. f. d. ges. Neurol. u. Psychiat. **155**:416, 1936.

6. Bailey, P.: Cruveilhier's "Tumeurs perlées," Surg., Gynec. & Obst. **31**:390, 1920.

Calcification was an extremely rare feature in the cases of intracranial epidermoid reported in the literature; in fact, only 1 definite case has been reported.[7] In addition, a case of cerebral cyst containing cholesterol crystals and covered by a calcareous capsule was reported by Craig and Kernohan,[8] but no cellular elements were present to indicate the true nature of the tumor. It is, therefore, surprising that 4 of the 6 intracranial epidermoids which we have encountered were extensively calcified. On the basis of previous experience with calcification in these tumors, we have been able to make a tentative preoperative diagnosis in our most recent case from the appearance of the calcification in roentgenograms.

Symptoms.—The clinical history is characterized by its long course, with very slow progression of symptoms. In our 4 clinical cases the average duration of symptoms before the patient's admission to the hospital was ten years.

It has been stressed that mental symptoms are of frequent occurrence. Such symptoms were present in 57 per cent of the cases of intracranial and in 14 per cent of the cases of intradiploic epidermoid collected from the literature by Mahoney.[5] Busk,[9] in 1855, and Wilks,[10] in 1859, stated that this type of tumor occurred only, or most frequently, in psychotic persons. Critchley and Ferguson,[11] however, in reporting 8 cases, did not find the mental state grossly affected in any of their patients and concluded that mental symptoms were absent because all of their patients were operated on relatively early.

The clinical features, therefore, that tend to distinguish the epidermoid from other intracranial tumors are: (1) the greater incidence of mental symptoms simulating those of a lesion of the frontal lobe regardless of the location of the epidermoid; (2) slow progression of symptoms; (3) extensive calcification of the periphery of the tumor, and (4) in the suprasellar type, slowly progressive optic nerve atrophy,

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7. Horrax, G.; Yorshis, M., and Lavine, G. R.: Calcified Intradural Cholesteatoma of Unusual Size in a Patient Showing Manic Depressive Symptoms, Arch. Neurol. & Psychiat. **33**:1058 (May) 1935.

8. Craig, W. M., and Kernohan, J. W.: Cerebral Cysts, J. A. M. A. **102**:5 (Jan. 6) 1934.

9. Wedl, C.: Cholesteatoma, in Rudiments of Pathologic Histology, translated and edited by G. Busk, London, Sydenham Society, 1855, p. 474.

10. Wilks, S.: Two Cases of Cholesteatomatous Tumour of the Brain, Tr. Path. Soc. London **10**:24, 1859.

11. Critchley, M., and Ferguson, F. R.: The Cerebrospinal Epidermoids (Cholesteatomata), Brain **51**:334, 1928.

with bitemporal hemianopia in a young person, without signs of pituitary insufficiency.[12]

Diagnosis.—A correct preoperative diagnosis of a cerebral epidermoid was first made in 1932 by Nagel,[13] when he found the characteristic tumor cells in the spinal fluid. There are numerous reports in the literature of spontaneous rupture of epidermoids into the ventricle or the subarachnoid space, producing in some cases sudden death and in others only meningitis, with appearance of cholesterol crystals or tumor cells within the spinal fluid.

The roentgenologic examination is frequently diagnostic. In the plain films extensive calcification about the surface of the tumor or cyst has been, in our experience, a frequent finding. It was demonstrated in cases 1, 2, 4 and 5 reported here.

The intraventricular epidermoid presents a characteristic encephalographic appearance, consisting of ventricular displacement associated with replacement of most of the normal ventricular gas by a more extensive area of irregular collections or streaks of air. This characteristic roentgenographic appearance was first reported by Krieg [14] in 1936 and then by Dyke and Davidoff [15] in 1937. It was confirmed by Weinberger [16] in another case reported in 1938. In our case 3 similar ventriculographic features were presented.

Olivecrona [12] suggested that in the presence of signs of a suprasellar lesion with a normal-sized sella but with large optic foramens and pressure absorption of the anterior clinoid processes and the sulcus chiasmaticus a suprasellar epidermoid is to be suspected.

Treatment.—Surgical removal is of course the only effective treatment, but, unfortunately, owing to their position along the base of the brain, in or near the midline, many epidermoids are inaccessible for total removal. Incomplete removal may be followed by a long survival period.[17] Both Cushing and Olivecrona emphasized that these tumors are expansive and spread into every crevice in the vicinity. Since the suprasellar epidermoid forms intimate relations with the large blood

12. Olivecrona, H.: On Suprasellar Cholesteatoma, Brain **55**:122, 1932.

13. Nagel, F.: Beitrag zur Liquorzelldiagnostik, Nervenarzt **6**:197, 1933.

14. Krieg, W.: Aseptische Meningitis nach Operation von Cholesteatomen des Gehirns, Zentralbl. f. Neurochir. **1**:79, 1936.

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16. Weinberger, L. M.: Intracerebral Epidermoid Tumors—A Characteristic Encephalographic Finding, J. Mt. Sinai Hosp. **5**:565, 1938.

17. Horrax, G., in discussion on King.[25] Cairns, H.: The Ultimate Results of Operations for Intracranial Tumors, Yale J. Biol. & Med. **8**:421, 1936.

vessels and the optic chiasm and often herniates into many clefts and crevices, Olivecrona cautioned against any attempt to remove the capsule. He expressed the belief that the optic nerves should not be searched for except when the anatomic relation of the chiasm and other important structures in this region are perfectly clear. When the capsule is not removed recurrence is inevitable.

Aseptic Meningitis.—The contents of an epidermoid are apparently irritating, as evidenced by reports of adhesions about the tumor, as well as by many reports of aseptic meningitis following operation on the tumor. Olivecrona,[12] one month after cleaning out the contents of a suprasellar epidermoid, performed a second operation because of headache and fever. He found the opening previously made in the capsule closed by adhesions. When they were separated a large amount of thick pus, sterile in smears and culture, was evacuated. In another of his cases, after removal of an epidermoid of the lateral ventricle fever and increased intracranial pressure, with a turbid but sterile spinal fluid, were present for several weeks. In still another case an epidermoid of the fourth ventricle ruptured spontaneously to produce fatal aseptic meningitis.

Krieg [14] reported 2 cases in which aseptic meningitis occurred after removal of an epidermoid. There developed fever, which continued for several weeks, stiffness of the neck, headache, increased cerebrospinal fluid pressure and pleocytosis, with a count as high as 20,000 cells per cubic millimeter of spinal fluid. Cultures were sterile. After these experiences, Krieg reviewed the literature for evidence of aseptic meningitis following spontaneous rupture or operative removal of an epidermoid. Reports of 2 cases were found in which the tumor had ruptured into the third ventricle, producing sudden death. Four other cases were discovered in which a rupture of the epidermoid with diffusion of the contents through the subarachnoid spaces produced no severe symptoms. Krieg found evidence of postoperative aseptic meningitis in cases reported by Hofmeister, Armour and Foerster. He also found reports of cases in which there was inflammation, or even pus, about the tumor, although no rupture or operation had occurred. Critchley and Ferguson [11] reported 3 cases of meningitis following operation for epidermoid.

Operative Mortality.—In general, the mortality following operation for intracranial epidermoid has been high, although some surgeons have reported reasonably low figures. Of 142 cases of intracranial epidermoid collected by Mahoney,[5] death occurred without operation in 17 per cent. In 30 per cent of cases in which operation was done the patient did not

survive. Lereboullet [18] reported 8 collected cases of epidermoid cyst of the posterior fossa, in only 1 of which operation was successful. Alpers [4] reported 8 cases of intracranial epidermoid in which operation was performed, with 6 recoveries (25 per cent mortality). Findeisen [19] collected from the literature 200 cases of epidermoid of the pontile angle, in 35 of which operation was performed, with postoperative death in 20, or 57 per cent. From the Tönnis' clinic he recorded operation in 10 cases of intracerebral epidermoid, with 2 deaths (20 per cent mortality). Love and Kernohan [20] reported 7 cases of intradural epidermoid tumor, with 1 postoperative death (14 per cent mortality).

Report of Cases.—There are 8 cases in this group. Two were encountered at autopsy and 6 at operation. In 4 of the latter the tumor was intracranial and in 2 intradiploic.

CASE 1.—*Bilateral blindness for six years. Convulsive seizures for two years. Calcified mass above the sella turcica revealed in roentgenogram. Partial removal and evacuation of an epidermoid. Death two and a half years later. Necropsy.*

M. O. was first admitted to the University Hospitals on Oct. 31, 1931, complaining of drowsiness. When she was approximately 2½ years old her eyes began to cross. She was otherwise apparently active and precocious. At this time her vision began to fail, so that by the age of 4 years she was completely blind. When she was 3½ years of age, sick headaches developed, occurring every two weeks and lasting from twenty-four to seventy-two hours. When 8 years of age she began to have convulsive seizures, which continued up to the time of admission to the hospital, two years later. Epistaxis at times followed these seizures.

Physical examination revealed a blind but otherwise normal child. There was bilateral primary optic nerve atrophy. Roentgenograms of the skull showed definite evidence of increased intracranial pressure and a calcified mass in and above the sella turcica (fig. 1).

A diagnosis of craniopharyngioma was made. It was decided that since the patient had been blind for six years but was otherwise comfortable, operation was not indicated. She was discharged but was readmitted two months later, with otitis media. After a short stay in the hospital she was again discharged, returning again eighteen months later, when 11 years of age, because of sudden onset of status epilepticus. For two months prior to the last admission the child had manifested marked somnolence, sleeping thirteen to fourteen hours a day. She also had projectile vomiting once or twice weekly. Examination at this time revealed that the patient was slightly confused. There was spontaneous nystagmus. The deep reflexes were slightly more active on the left than on the right. Roentgenograms were essentially the same as before.

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18. Lereboullet, J.: Les tumeurs de quatrieme ventricule, Paris, J. B. Baillière & fils, 1932.

19. Findeisen, L.: Das Cholesteatom des Brückenwinkels, Arch. f. klin. Chir. **189**:490, 1937.

20. Love, J. G., and Kernohan, J. W.: Dermoid and Epidermoid Tumors (Cholesteatomas) of Central Nervous System, J. A. M. A. **107**:1876 (Dec. 5) 1936.

Operation.—A right transfrontal craniotomy was performed; as the right frontal lobe was elevated it was observed to be adherent to the dura along the sphenoid ridge. When these adhesions were separated, the anterior extent of the tumor was exposed. The right optic nerve was a flat ribbon, appearing as a fibrous band over the surface of the cyst. It was severed, the cyst opened and approximately 3 ounces (89 cc.) of straw-colored fluid and cholesterol crystals evacuated. On the inner wall of the cyst there were calcified projections, while elsewhere the wall was smooth, although the cyst had spread about various structures at the base of the brain so that these structures projected as irregularities in the contour of the inner wall.

Convalescence was not uneventful. On the second and tenth days after operation the patient had convulsive seizures, followed by high fever. Again, on the seventeenth postoperative day her temperature rose to 102 F. She was given a

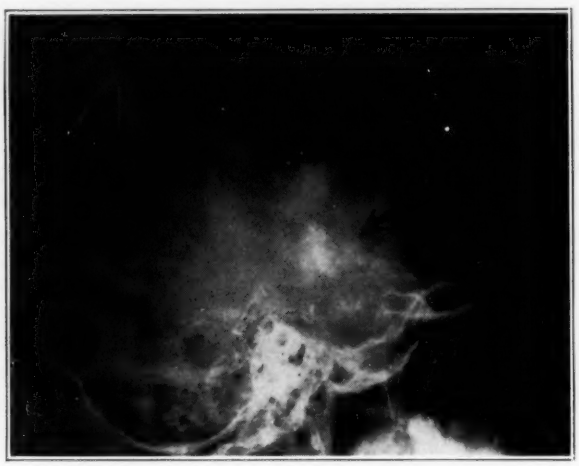

Fig. 1 (case 1).—Roentgenogram, showing calcified suprasellar epidermoid.

course of roentgen therapy and was discharged from the hospital on the fifty-fifth day after operation.

Two and one-half years later she returned, with erysipelas. The interval history revealed that she had had occasional epileptiform seizures. After nineteen days in the hospital she was discharged, but returned fourteen days later in coma. A few days before this admission seizures had become more frequent, and on the day of admission she became confused and then comatose. She died after thirty-three days in the hospital, without regaining consciousness.

Necropsy.—A large, calcified, cystlike mass lay in the midline at the base of the brain and produced enlargement of the sella, the latter measuring 4 by 3.5 cm. (fig. 2). The neoplasm was well encapsulated and, for the most part, was easily separated from the brain. It measured 8 by 6 by 5 cm. and was cystic in some areas and firm and nodular in others. Only the left optic nerve could be identified,

and it was extremely flattened over the interior border of the tumor. The rest of the optic structures were not isolated, since they were incorporated into the tumor. On cut section the cystic parts of the growth contained large masses of yellowish, necrotic, partially calcified material.

Histologically, the cyst wall was composed of a dense layer of connective tissue that had already undergone partial hyalinization and calcification. Along the inner surface of this fibrous layer were scattered numerous epithelial cells, representing the stratum granulosum of the epidermoid. The center of the tumor was composed of broken-down debris, consisting of fatty material and cholesterol crystals. Scattered among this debris were large sheets of very clear, large, regular cells that contained no nuclei. They probably represented the so-called woody, plantlike cells seen in epidermoids.

Diagnosis.—The diagnosis was suprasellar epidermoid.

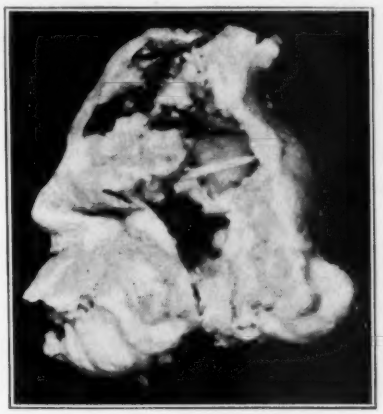

Fig. 2 (case 1).—Suprasellar epidermoid.

CASE 2.—*Left hemiplegia for thirteen years. Epileptiform seizures for four years. Large calcified tumor in right cerebral hemisphere revealed in roentgenograms. Removal of epidermoid. Patient well three years after operation.*

M. T., an 18 year old Mexican girl, first had weakness and intermittent contractions in the left arm and hand when 5 years of age. Some two months later these contractions spread to the left side of the face, and weakness progressed to produce complete paralysis of the left hand and severe paresis of the left leg. Flexion contracture of the left wrist and inversion of the left foot developed. Four years before admission, at the age of 14, she began to have epileptiform seizures, which were more frequent in winter than in summer. They were of grand mal type and were preceded by vertigo. More recently headache and nausea had developed.

Examination at the time of admission revealed left spastic hemiplegia with contractures. There was complete paralysis of the left hand and foot, but incomplete paralysis of the arm, shoulder and thigh muscles. Sensory reception to all types of stimuli was decreased on the left side. Visual acuity was 20/20 in the right eye and 20/25 in the left eye. There was slight primary optic nerve atrophy

of the temporal side of the disk in the left eye. The peripheral fields were normal, but the central fields showed paracentral scotoma bilaterally.

Roentgenograms revealed a large calcified mass in the medial portion of the right hemisphere of the cerebrum (fig. 3).

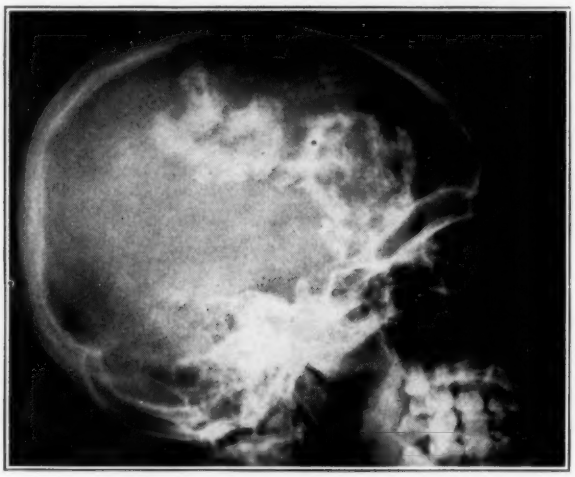

Fig. 3 (case 2).—Roentgenogram, showing calcified intracerebral epidermoid.

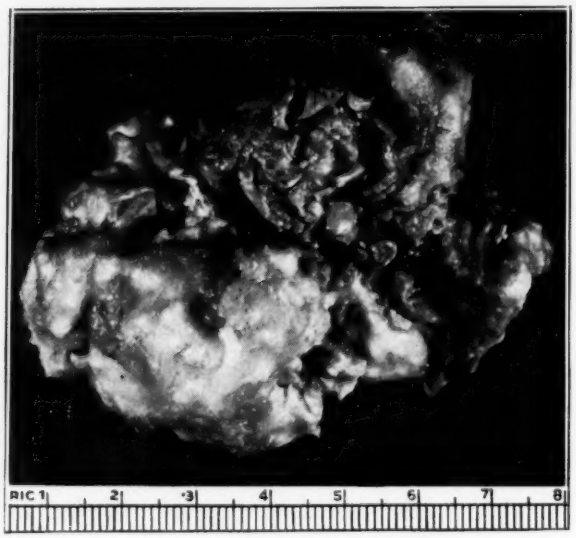

Fig. 4 (case 2).—Calcified intracerebral epidermoid.

First Operation (Oct. 6, 1938).—A very large flap over the left hemisphere of the cerebrum was reflected and replaced.

Second Operation (Oct. 25, 1938).—The flap was again reflected and the dura opened. A very irregular, calcified tumor protruding through the cerebral cortex was exposed. At no point was this tumor attached to the meninges. It was not

infiltrating but was adherent to the surrounding cerebral tissue. No blood vessels passed into the tumor, which consisted of a calcified shell and a grumous center. The mass was easily removed by dividing it in the middle, where it came to the surface, so that each half could be shelled out with minimum destruction of cerebral tissue. The right cerebral hemisphere collapsed after removal of the tumor.

Pathologic Report.—The tumor consisted of a large, irregular, calcified mass, measuring 8 by 6 by 4 cm. and containing a soft necrotic center, composed of a homogeneous, structureless material (fig. 4). Cross section of the capsule revealed a heavy layer of calcification and hyalinization, which probably represented the stratum durum. In certain regions a distinct layer of stratified epithelial cells was

Fig. 5 (case 2).—Microscopic appearance of an epidermoid.

observed (fig. 5). These cells were very large, with nuclei and definite intracellular bridges. No keratohyaline granules were present.

The diagnosis was epidermoid.

Postoperative Course.—The patient made an uneventful recovery and was discharged from the hospital twenty days after removal of the tumor. During the three years that have elapsed since operation there have been slight improvement in movements of the muscles of the left forearm and definite improvement in muscle strength in the left leg. The paracentral scotomas in the visual fields have disappeared, and the mental reactions are quicker. The patient has had one epileptiform seizure.

CASE 3.—*Symptoms for twelve years, consisting of personality disturbance, paralysis of left side and signs and symptoms of increased intracranial pressure.*

Encephalogram, with signs typical of intraventricular epidermoid. Operation and removal of tumor. Aseptic meningitis and death.

C. C., a 67 year old man, was admitted to the University Hospitals on Dec. 16, 1938. His judgment began to be impaired in 1926. Eight years prior to admission he began to have difficulty in the use of his left hand, and two years later, in the use of his left foot. By 1937 extensive left-sided paresis had developed. He found it impossible to concentrate, could not remember recent events and became untidy about his dress and living quarters.

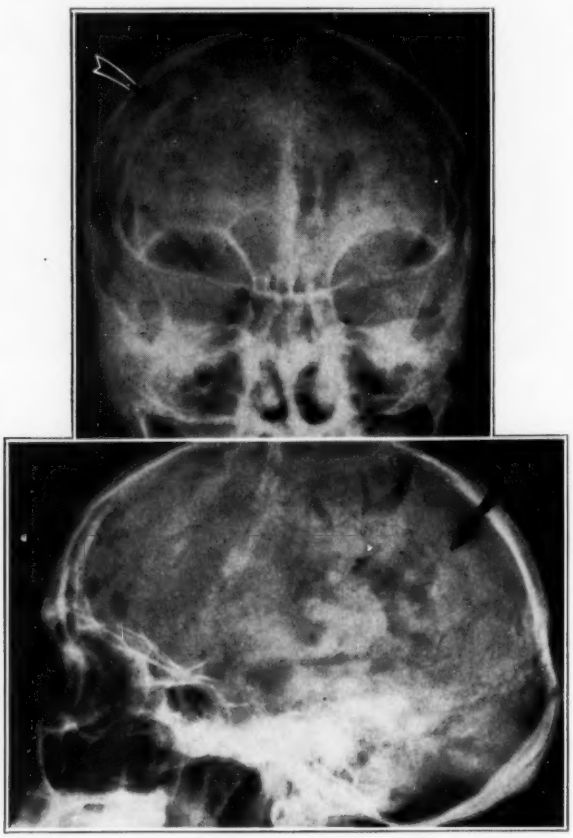

Fig. 6 (case 3).—Encephalograms in a case of intraventricular epidermoid.

Neurologic examination showed euphoria, extreme loss of memory and disorientation as to time and place, but retention of vocabulary. The left pupil reacted sluggishly to light; left homonomous hemianopia and early bilateral optic nerve atrophy were present. There was almost complete spastic paralysis of the left side of the body, with positive toe signs. Superficial sensation was also impaired on the left side. Examinations of the spinal fluid gave results within normal limits. The spinal fluid pressure was 9 mm. of mercury. Roentgenograms showed decalcification of the clinoid processes and calcification of the pineal gland, which was displaced to the left.

An encephalogram (fig. 6) revealed a large cystic area, filled partially with air and partially with a tumor mass, situated in the region of the right parietal

and occipital lobes and occupying the right ventricle, but extending far beyond the confines of the normal ventricle. The left lateral ventricle was displaced to the left. This appearance is characteristic of an epidermoid in the lateral ventricle.

Operation.—With intratracheal gas anesthesia, a right parieto-occipital craniotomy was performed. The tumor did not appear on the surface, but a shallow cortical incision through thin, flattened, soft convolutions opened into a cystic tumor, the contents of which consisted of amorphous material and cholesterol crystals. The wall was composed of a thin friable membrane, adherent to the cerebral tissue. The right lateral ventricle was filled with tumor, which projected across the midline into the posterior part of the left lateral ventricle. The contents of the cyst were sucked out, and the entire wall was removed except for a small portion in the posterior horn of the left lateral ventricle.

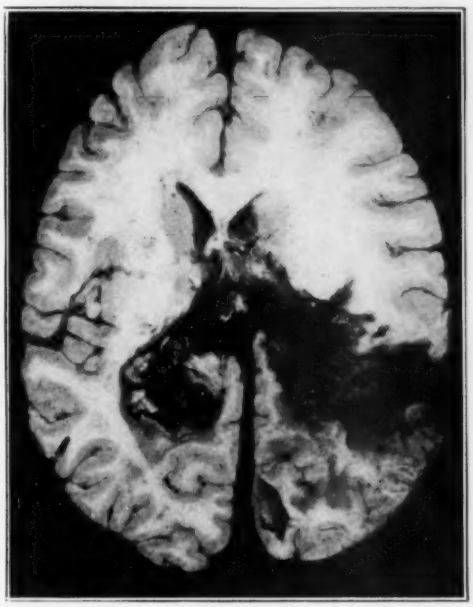

Fig. 7 (case 3).—Autopsy specimen of intraventricular epidermoid. An operative defect is seen on the right side and crossing the midline. The unremoved epidermoid lies in the posterior part of the left lateral ventricle.

Course.—For several days after operation the patient appeared to be on the way to recovery. He was conscious and rational but had a temperature from 101 to 104 F., with a somewhat increased pulse rate. This fever and rapid pulse continued until death, seventeen days after operation. The spinal fluid obtained from multiple punctures proved to be sterile.

Necropsy.—Horizontal sections through the brain revealed a large operative defect, measuring 6 by 13 cm., within the right parietal lobe. In the anteromedial portion of the left occipital lobe there was a well circumscribed, pearly tumor, measuring 3 by 2 cm. This tumor was a continuation of the operative defect from which the right half of this tumor had been removed. The posterior portions of both lateral ventricles had been filled with extensions of this single tumor mass (fig. 7).

Microscopic examination revealed the typical structure of an epidermoid. Central necrotic material was surrounded by a layer of epithelial cells. These cells were in direct contact with the surrounding brain tissue, the stratum durum not being present. The epithelial layer, or the stratum granulosum, was composed of stratified cells, the innermost containing numerous keratohyaline granules (fig. 8). This epithelial layer was limited inwardly by a heavy, structureless band of tissue, which tended to blend with the necrotic center. A few cholesterol crystals were present within the central debris.

The diagnosis was that of epidermoid.

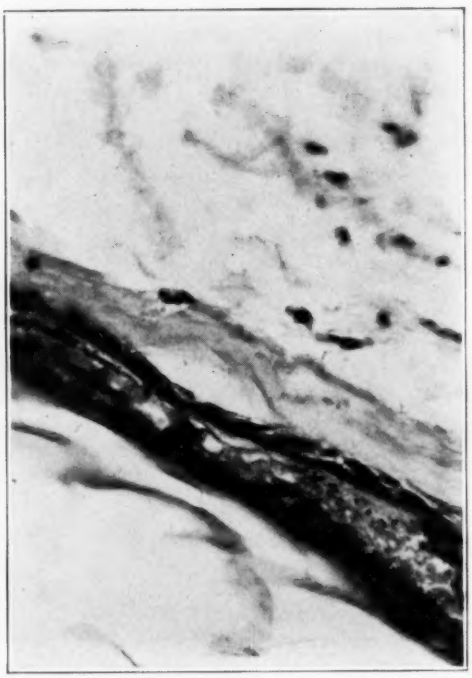

Fig. 8 (case 3).—Microscopic appearance of an epidermoid.

Insertion of an intradural drain for twenty-four hours, a procedure which we are now using after most intracranial operations, might have prevented this fatality. Certainly, it would seem to be advisable to establish drainage after removal of intracranial cholesteatoma.[20]

CASE 4.—*Epileptiform seizures for nine years. Calcified mass in right temporal lobe revealed in roentgenograms. Operation, with removal of calcified epidermoid from region of right hippocampus. Relief from seizures, but left hemiplegia persisted.*

A. H., a 44 year old man, was admitted to the University Hospital clinics in February 1940, with a history of having been well until nine years before, when

seizures began to develop. At first they consisted of petit mal attacks but gradually became more severe and more frequent. At the time of his admission he was having as many as three grand mal seizures daily. Recently, he had also had periods of confusion, during which he would walk, more or less nude, out on the highway and try to catch a ride or would wander far from his place of work.

Physical and neurologic examinations revealed no abnormality except some constriction in the upper temporal portion of the visual field of the left eye. Roentgenograms of the skull demonstrated a mass in the right temporal lobe, which was calcified in its periphery and appeared to be a densely calcified cyst (fig. 9). Among the suggested diagnoses was that of epidermoid.

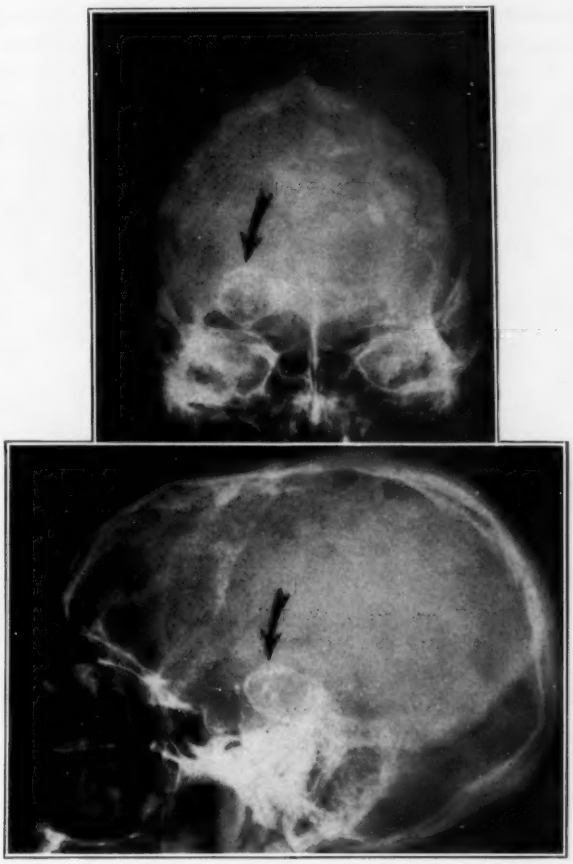

Fig. 9 (case 4).—Encephalograms, showing calcified epidermoid in the right gyrus hippocampi.

Operation.—On March 9 a right temporoparietal flap was reflected, the right temporal horn of the ventricle tapped, the lobe elevated and parts of the gyrus fusiformis and hippocampus removed to uncover a subcortical calcified cyst in the

gyrus hippocampus. The cyst was easily removed by gently brushing cerebral tissue from it. It was avascular except at its inner side, where one artery seemed to pass into it.

Course.—After operation the patient had complete left hemiplegia (injury to the internal capsule). Sufficient movement returned to the left leg to enable him to walk, in spite of a persistent foot drop. The weakness of the left side of the face improved, leaving only slight paresis of the lower part. Tendon reflexes remained hyperactive on the left side, and the toe signs were positive. Superficial sensibility was reduced over the entire left side of the body. There was homonomous hemianopia. The right pupil varied in size, without any change in focus or in response to light stimulation, for several days after operation and since then has remained smaller than the left. When last seen, three months after operation, the patient had had no seizures but complained of paralysis of the left arm and of burning pain in the entire left side of the body.

Pathologic Report.—The tumor was a firm, rounded mass, measuring 2 by 2 by 4 cm. (fig. 10), and was filled with a homogeneous, necrotic material, which contained areas of cholesterol crystals. The outermost portion of the capsule of this

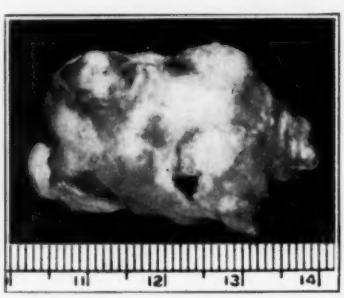

Fig. 10 (case 4).—Calcified epidermoid from the right gyrus hippocampi.

growth was composed of collagenous tissue, in which hemorrhage and areas of calcification were seen. The inner layers contained stratified epithelium, which had partially undergone degeneration and calcification.

The diagnosis was epidermoid.

CASE 5.—*Paralysis of the left arm since childhood. Paresis of left leg for two years. Admission to hospital in coma. Death from miliary tuberculosis. Intracranial epidermoid revealed at autopsy.*

T. O., a 66 year old man, an Indian, was admitted to the hospital for the first time in July 1940 because of generalized dermatitis. The history was hard to obtain because of the patient's language difficulty. As far as could be determined, he had had paralysis of the left upper extremity since infancy. The weakness of the left lower limb appeared in 1938, and the paresis had progressed fairly rapidly during the past two years.

Examination showed atrophy and complete spastic paralysis of the left side, with hyperactive deep reflexes and sustained clonus. After treatment for the

dermatitis he was discharged; he returned to the hospital six months later, in coma, and died shortly after admission.

Necropsy.—External examination of the brain revealed a decrease in size of the entire right cerebral hemisphere. Horizontal sections disclosed a large irregular, nodular mass, measuring 4.5 by 2 cm., lying within the right lateral ventricle and filling its anterior horn and the anterior half of the body. This mass was extremely calcified and was well demarcated from the surrounding brain tissue except at one point in the lateral wall of the ventricle. The overlying cortex was reduced to a layer of less than 5 mm. in thickness (fig. 11 *A* and *B*). After removal the tumor was sectioned with a bone-cutting forceps. It was almost completely calcified, only a few tiny cavities being filled with a necrotic material.

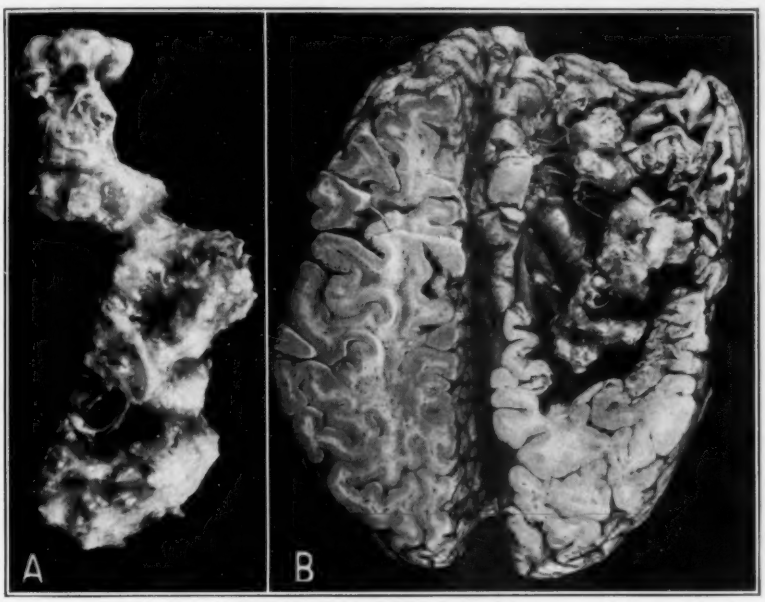

Fig. 11 (case 5).—*A* calcified intracerebral epidermoid. *B* calcified intracerebral epidermoid lying in the ventricle.

Histologic sections after decalcification revealed most of the tumor to be composed of hyalinized and calcified material, with obliteration of all cellular elements. The small cavities were filled with cholesterol crystals.

The diagnosis was epidermoid.

CASE 6.—*Sudden death. Bilateral symmetric cholesteatoma of the lateral ventricles revealed at autopsy.*

A. Y., a man aged 45 years, was found unconscious on the street and was brought to the hospital on Dec. 22, 1938, where he died a few hours later.

Autopsy.—Two very symmetric tumor masses, each measuring 5 by 2 cm., were situated in the bodies of the lateral ventricles and were joined medially within the partially obliterated third ventricle. Each tumor was attached to the choroid plexus (fig. 12). The tumors were slightly nodular and very firm.

Microscopic sections showed these tumors to be composed almost entirely of cholesterol crystals. Scattered among the crystals were numerous foci of mononuclear cells and some foreign body giant cells. There was paucity of blood vessels, although a few areas of free erythrocytes could be seen among the fatty elements. The periphery of the tumor was composed of a thin layer of fibrous tissue that was mostly hyalinized and partially calcified. Some calcium granules were also deposited within the center of the mass. No epithelial elements were detected in any of the sections.

The diagnosis was cholesteatoma.

Fig. 12 (case 6).—Bilateral intraventricular cholesteatoma.

Although this type of tumor is fairly common in the horse, its occurrence in man is unusual. The tumor in the horse is almost always bilateral and seems to arise from the choroid plexus. Usually the masses float loosely within the lateral ventricles, being merely attached to the choroid plexus. Often the neoplasm produces no symptoms in the horse, although in some instances stupidity, "staggers," or even paralysis results.

Histologically, this tumor differs from the true epidermoids chiefly in the lack of epithelial tissue. For this reason, McFadyean [21] suggested that it be classified with the psammomas, even though it was not identical in structure with the tumors of this type in man. Because of the structure of this tumor in the horse, with its predominant cholesterol structure, it appears best to classify the neoplasm as cholesteatoma but to keep in mind that it probably differs from the usual epidermoid seen in man.

INTRADIPLOIC EPIDERMOID

The first case of primary cranial epidermoid, according to Quade and Craig,[22] was reported by Müller in 1838. Bucy,[23] in 1935, was able to find only 13 similar cases reported in the literature. He preferred to call the tumor intradiploic epidermoid. It is much less common than the intracranial type. Mahoney [5] found only 23 cases, as contrasted with 122 cases of intracranial epidermoid reported in the literature up to 1936.

This tumor arises in the diploe and by growth expands both tables of the skull. Its structure is similar to that of the intracerebral lesions. The contents consist of whitish sebaceous material composed of cholesterol crystals and fragments of structureless cells. The cyst wall usually contains the same layered structure as that described for the intracranial epidermoid. The presence of a layer of stratified squamous epithelium is considered essential for a diagnosis of this tumor type.

The diploic epidermoid may become very large and compress, or even deform, the cerebral hemisphere without producing neurologic signs. The majority of these epidermoids merely present the picture of a very slow-growing, soft tumor mass of the skull, even though Mahoney [5] found that in 14 per cent of collected cases of diploic epidermoid psychic disturbances were produced.

Diagnosis.—The roentgenologic appearance is characteristic. This was first pointed out by Cushing [24] in 1922 and soon thereafter was utilized by King [25] to make the first preoperative diagnosis of a diploic epidermoid. In roentgenograms taken so that the greatest diameter of the defect is shown the margins are scalloped, dense and clearcut. This

21. McFadyean, J.: Cholesteatoma in the Brain of a Horse, J. Comp. Path. & Therap. **24**:137, 1911.

22. Quade, R. H., and Craig, W. M.: Unusual Dermoid and Epidermoid Cranial Cysts, Proc. Staff Meet., Mayo Clin. **14**:459, 1939.

23. Bucy, P. C.: Intradiploic Epidermoid (Cholesteatoma) of the Skull, Arch. Surg. **31**:190 (Aug.) 1935.

24. Cushing, H.: A Large Epidermal Cholesteatoma of the Parietotemporal Region Deforming the Left Hemisphere Without Cerebral Symptoms, Surg., Gynec. & Obst. **34**:557, 1922.

25. King, J. E. J.: Extradural Diploic and Intradural Epidermoid Tumors (Cholesteatoma), Ann. Surg. **109**:649, 1939.

eburnated bony margin is a most characteristic feature. The inner table of the skull is usually more involved than the outer.

Treatment.—This tumor must be totally removed to effect a cure. The dura is not penetrated, but the wall of the cyst is often intimately adherent to its surface and must be removed. Careful curetting seems to be the most satisfactory and the most common method of removal, but in some cases the outer layer of the dura has been removed with the cyst.[20] If the outer table is not penetrated, the tumor may be elevated in a bone flap and removed intact from its inner surface.[23]

CASE 7.—*Lump on left side of forehead for four years, appearing after injury. Epidermoid revealed in roentgenogram. Operation, with removal.*

M. F., a 24 year old woman, four years before her admission to the University Hospitals bumped her head against the windshield of an automobile. A few weeks later she noted a lump on the left side of her forehead. This lump remained small and gave her no trouble for three years. For the past year it had grown larger, become tender and produced a "drawing sensation" across her forehead.

Examination on admission, on May 23, 1939, revealed essentially nothing abnormal except for a tumor, 3 cm. in diameter, in the region of the left frontal eminence. Roentgenograms demonstrated a rarefied area with sclerosis of its margins, suggestive of a diploic epidermoid.

Operation.—A coronal incision was made above the hair line and the scalp reflected to expose the lesion above the left orbit. The outer table of the skull, as well as the bony wall of the frontal sinus, had been completely eroded. The inner table of the skull was eroded over a much smaller area, allowing the cyst wall to come in contact with the dura. The content of the cyst was evacuated, and its thin membranous wall was stripped and curetted out. Complete removal was accomplished without breaking through the dura or into the frontal sinus. This left the patient with a pulsating defect in her skull approximately 3 cm. in diameter. This defect was obliterated four months later by reopening the former incision and again reflecting the flap, as at the first operation. A portion of the outer table of the skull was removed with a Gigli saw from the posterior part of the exposed skull and put in the defect, thus producing a satisfactory cosmetic result.

Pathologic Report.—Microscopic sections revealed chiefly masses of necrotic tissue, with no cellular elements. In some areas the tissue had a peculiar layered appearance, with small open spaces resembling injured and compressed cells.

The diagnosis was epidermoid.

CASE 8.—*Small mass under scalp in the right parietal region. Gradual increase in size over a period of months. Area of rarefaction, with sclerotic margins, revealed in roentgenogram. Operation, with removal.*

D. K., a 1 year old boy, had been in good health since birth. Four months before admission to the hospital, on April 17, 1941, his mother noticed a small mass beneath the scalp over the right parietal region. This mass steadily increased in size but remained asymptomatic.

Examination revealed a nontender mass, about 3 cm. in diameter, involving the skull in the right parietal region, about 2 cm. to the right of the midline. The skin over the mass was freely movable. Roentgen examination showed a circumscribed area of rarefaction with sclerotic margins. The diagnosis was epidermoid.

Operation.—A curved incision extending over the tumor was made, and a flap was turned down to expose the bone. The tumor had eroded through both the outer and the inner plate. A trephine opening was made at the inferior margin, the dura freed from the bone and the tumor removed, without injuring the dura. In the superior part of the lesion the dura showed evidence of invasion by tumor. It was felt that because of the superficial nature of the dural involvement, coagulation of the dura, which was performed, would be most satisfactory and would probably be adequate to destroy the tumor elements. The postoperative course was uneventful, and the child was discharged on the eleventh postoperative day.

Pathologic Report.—Microscopic sections revealed most of the tumor tissue to be composed of fibrous connective tissue, adipose tissue and many structureless cells and fibers. In scattered areas, especially at the periphery, there were small islands of compressed cellular elements which were impregnated with tiny calcium granules. Study under high magnification revealed these cells to be partially obliterated epithelium. Hyalinization and necrosis had occurred, but no cholesterol crystals could be found.

The diagnosis was epidermoid.

EPIDERMOID OF THE SPINAL CANAL

Cases of epidermoid tumors in this location are rare. Of 142 cases of epidermoid collected from the literature by Mahoney,[5] only 7 were of this type. One such case which we encountered has been included in a separate report on mixed tumors of the spinal canal [26] and is only briefly reviewed at this time.

CASE 9.—*Dermal sinus since birth. At 2 years of age, appearance of disturbance in gait, fever and stiff neck. Repeated operations for drainage of an epidermal abscess in the sacral region, with removal of pus and cholesterol-like crystals. Extensive excision of the dermal sinus and abscess cavity. Histologic diagnosis: epidermoid.*

M. S., a girl, was born Oct. 12, 1936, with a dermal sinus over the sacrum. She was admitted to the University Hospitals in June 1938, because of irritability, restlessness, nausea and vomiting, of a few days' duration. Disturbance in gait had been present for some time. On examination the child cried when placed on her back but was quiet when lying on her side or abdomen. She had fever, stiff neck and a bilateral Kernig sign. The spinal fluid on repeated examinations contained from 1,000 to 3,000 cells per cubic millimeter. In an attempt at spinal puncture, two months after the patient's admission, pure pus was obtained. This led to operation for epidural abscess. However, an intradural collection of pus and cholesterol-like plaques was found within a very thin-walled sac among the roots of the cauda equina. Since the wound continued to drain, a second and a third operation was performed. At the last exposure, a piece of the sac obtained for histologic study showed stratified squamous epithelium. It was then realized that the dermal sinus over the sacrum and the sac in the upper lumbar region were one continuous process. On May 1, 1940 complete flaccid paralysis of the lower limbs suddenly developed, necessitating a fourth operation for drainage. This was followed by partial recovery. In July 1940, after the acute inflammation had subsided, a fifth operation was performed to excise the epithelium-lined tract.

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26. French, L. A., and Peyton, W.: Mixed Tumors of the Spinal Canal, Arch. Neurol. & Psychiat. **47**:737 (May) 1942.

Beginning with an excision of the dermal sinus over the first sacral vertebra, the laminectomy was continued upward to include the twelfth thoracic vertebra, but still the upper extent of the epithelium-lined tract was not reached. The removed segment consisted of 12 cm. of tract, beaded at many points with pearly nodules, the largest being 1.5 cm. in diameter, which contained cholesterol.

The patient regained some of her sphincter control and now, fifteen months after the operation, walks with a slight limp. The wound is completely healed.

Pathologic Report.—Microscopic sections of the tissues removed in 1939 revealed large masses of fibrous tissue and chronic granulation tissue. Small islands of stratified squamous epithelium were scattered throughout. The tissue removed in 1940 contained small cystlike structures lined with a layer of stratified epithelium. The cysts contained a small amount of necrotic, structureless material.

The diagnosis was epidermoid.

DERMOID OF THE CENTRAL NERVOUS SYSTEM

An intracranial, intradural dermoid was described by Verratus in 1745,[27] long before the epidermoids were recognized. This tumor is less common than the epidermoid. According to Brock and Klenke,[28] in Cushing's 1,936 verified brain tumors there were 11 epidermoids, 3 dermoids and 5 teratomas. Among the 450 verified brain tumors at the New York Neurological Institute there were 4 epidermoids, 2 dermoids and no teratomas. Love and Kernohan [29] reported that the ratio of epidermoids to dermoids was 7:3. We have encountered 6 cerebral epidermoids and only 1 cerebral dermoid.

Structure.—The dermoid is usually a round or irregular multilocular mass situated within the cerebral hemisphere. It is not uncommonly multiple and is frequently associated with other congenital anomalies and developmental errors. The tumor is almost always cystic, the cyst being surrounded by a thin wall which demarcates it from the surrounding brain tissue. The cyst is filled with a liquid or semiliquid, "oily," yellowish material, which contains tangles of hair growing from the epidermal lining. Numerous nodular projections extend from the wall into the cyst and are called dermoid tufts. Sebaceous glands are numerous, especially along the hair follicles. Teeth and bone are rarely found within this tumor.

Clinical Features.—The symptoms and neurologic signs are similar to those produced by the epidermoids. The intracranial dermoid is slow growing and is frequently calcified.[29] It tends to occur near the midline

27. Verratus, cited by King.[25]

28. Brock, S., and Klenke, D. A.: A Case of Dermoid Overlying the Cerebellar Vermis, Bull. Neurol. Inst. New York **1**:328, 1931.

29. (*a*) Rand, C. W.: Intracranial Dermoid Cyst, Arch. Neurol. & Psychiat. **14**:348 (Sept.) 1925. (*b*) Horrax, G.: A Consideration of the Dermal Versus the Epidermal Cholesteatomas Having Their Attachment in the Cerebral Envelopes, ibid. **8**:265 (Sept.) 1922. (*c*) Gray, R. C.: Dermoid of the Cerebral Hemispheres, Minnesota Med. **22**:530, 1939. (*d*) Brock and Klenke.[28]

of the base of the brain but, unlike the epidermoid, does not occur in the cerebellopontile angle.[29b]

Report of a Case.—We have encountered only 1 case of intracranial dermoid. Since this case has been reported by Gray,[29c] only a brief comment will be made at this time.

CASE 10.—The patient, a 28 year old Indian, was admitted to the hospital on Jan. 23, 1931. For two years he had noticed progressive disturbance in his vision, writing and gait. When admitted he was confused and hallucinatory. Examination was unsatisfactory because of poor cooperation. There were no gross alterations in the motor or sensory system. Roentgenograms of the skull showed an area of calcification about 2 cm. to the right of the midline, immediately posterior to the frontal sinus.

Operation through a right frontal approach, with removal of part of the right frontal lobe, revealed a large cyst situated medial to the anterior horn of the right lateral ventricle. The cyst, filled with sebaceous material containing hair, was dumb-bell in shape and extended across the midline to involve also the left hemisphere. It had a smooth lining but showed some papillary growths, or dermoid tufts. All accessible portions of the cyst were removed. Recovery was uneventful, with some improvement in the patient's mental state. The patient died three months after leaving the hospital.

DERMOID OF THE SPINAL CANAL

Dermoid of the spinal canal is also rare. In the literature from 1875 to 1938 Elvidge and Boldrey [30] were able to find only 36 reported cases, to which they added 3 of their own. In all but 2 of the reported cases the tumor was subdural. More recently, Rasmussen and associates [31] reported 2 cases of dermoid and 1 of teratoma in a series of 557 verified intraspinal tumors. Most of the spinal dermoids are in the region of the cauda equina. Dysraphia is usually present. We have not encountered a case of dermoid of the spinal canal.

TERATOMA OF THE CENTRAL NERVOUS SYSTEM

Exclusive of epidermoids, Sweet,[32] in 1940, was able to collect from the literature 156 cases of intracranial dermoid, teratoid and teratomatous tumors. He expressed the belief that this whole group of interrelated tumors consists pathologically of a series of structures of gradually increasing complexity and that any attempt to separate them into subgroups must be at least arbitrary. He classified these tumors as follows: (1) dermoids, tumors containing only elements found in the epidermis

30. Elvidge, A. R., and Boldrey, E. B.: Dermoid Cysts of the Vertebral Canal, Tr. Am. Neurol. A. **64**:209, 1938.

31. Rasmussen, T. B.; Kernohan, J. W., and Adson, A. W.: Pathological Classification with Surgical Consideration of Intraspinal Tumors, Ann. Surg. **111**:513, 1940.

32. Sweet, W. H.: A Review of Dermoid, Teratoid, and Teratomatous Intracranial Tumors, Dis. Nerv. System **1**:228, 1940.

and corium; (2) teratoid tumors, mixed tumors which contain elements of one or two embryonic germ layers, thus including tissues other than those present in the skin, and (3) teratomas, tumors with elements of all three germ layers. Thus classified, Sweet found among cases of intracranial tumor reported in the literature 44 instances of teratoma, 50 of teratoid tumor and 62 of dermoid. Hosoi,[33] in 1930, collected 17 cases of intracranial teratoma from the literature and added 1 case of his own. He found 23 cases of intracranial teratoid tumor. Weber,[34] in 1939, found in the literature 64 cases of intracranial teratoma and teratoid and added 7 cases from the neurosurgical clinic of Berlin University.

Pathologic Structure.—Intracranial teratomas may vary from tiny nodules to large circumscribed cerebral masses. Ziskind and Schattenberg [35] recorded 1 case of a teratoma measuring 13 by 6 by 5.5 cm. Usually the tumor is a large, firm, irregular, nodular structure that may or may not contain cysts. It is well demarcated from the surrounding brain tissue. On section it shows a variable appearance. Some areas are reddish brown, while others appear yellowish and necrotic. Often, small bony or cartilaginous masses can be detected on gross inspection. Even teeth may be found in this tumor.

Histologically the teratoma is characterized by its tridermal character.

1. The ectodermal elements consist of nerve cells, neuroglia, stratified epithelium and dental elements. The nerve elements may appear as islands of brain tissue or consist of isolated clumps of nerve cells, neuroglia, giant glia cells and nerve fibers. All stages in the evolution of teeth may be made out. The areas of stratified squamous epithelium are frequently associated with the various skin appendages, namely, hair and glands.

2. The mesodermal elements are connective tissue, cartilage, bone, areolar tissue and fat. A connective tissue stroma often forms a large part of the tumor. Islands of bone and cartilage, as well as clumps of fat cells, are observed scattered irregularly throughout the tumor.

3. The endodermal elements are formed by islands of ciliated columnar and glandular epithelium, which may or may not assume definite tissue patterns resembling interstitial epithelium, salivary glands, thyroid, pancreatic tissue, etc.

Diagnosis.—Although teratoma may occur almost anywhere in the intracranial cavity, it is most common in the pineal region, the pituitary

33. Hosoi, K.: Teratoma and Teratoid Tumors of the Brain, Arch. Path. **9**:1207 (June) 1930.

34. Weber, E.: Die Teratome and Teratoide des Zentralnervensystems, Zentralbl. f. Neurochir. **4**:47, 1939.

35. Ziskind, J., and Schattenberg, H. J.: Teratoma of the Brain, Arch. Pediat. **56**: 347, 1939.

region and the posterior part of the posterior cranial fossa. Unlike the epidermoid, it is uncommon in the cerebellopontile angle.[32] The symptoms of intracranial teratoma or teratoid tumor are usually of many years' duration, but a more rapid onset of symptoms may occur, owing to obstruction of circulation of the cerebrospinal fluid or to malignant transformation occurring in some of the tissue elements of the tumor. Sweet [32] cited 7 cases in which the latter occurred.

Treatment.—Total removal is the only possible permanent cure. Fortunately, many teratomas and teratoid tumors are so situated that they can be totally excised, but those arising in the pineal gland are unfavorable for total removal. Only 1 of these has been successfully removed.[36]

Report of Cases.—We have encountered 2 cases of cerebral teratoma.

CASE 11.—*Convulsions at age of 7 months. Mental retardation. Inability to talk or walk. Tumor of left parietal lobe revealed in encephalogram. Teratoma removed at operation.*

J. J., a 2 year old infant, began to have convulsions after a slight injury to the head when 7 months old and continued to have daily epileptiform seizures up to the time of admission to the outpatient clinic of the University Hospitals, on Jan. 10, 1938. She had not learned to talk, had not been trained to control feces or urine, never showed interest in her surroundings and appeared unable to focus her eyes properly.

Neurologic examination revealed no paralysis or abnormal reflexes. The fundi were normal. Roentgenograms of the skull showed nothing abnormal. An encephalogram demonstrated the third and lateral ventricles to be much dilated, with a definite defect in the roof of the body of each lateral ventricle, suggesting a tumor in the posterior part of the lateral ventricles.

Operation (Feb. 14, 1939).—A large parietal flap of scalp, with its pedicle on the right side but extending across the midline, was reflected. The bone over the midline and several centimeters on each side were then removed and preserved, to be replaced at the completion of the operation. The dura was reflected up to the superior sagittal sinus bilaterally and the cerebral hemispheres separated in order to explore down along the falx. No tumor was encountered on the right, but on the left side a neoplasm was seen on the medial surface of the parietal lobe. It appeared to be approximately 3 cm. in diameter but was not well demarcated. Since the margins of the tumor could not be recognized with certainty, it was impossible to be sure that removal was complete. The patient recovered quickly from the operation but was not discharged until March 10, twenty-four days after operation, because fluid collected under the flap.

Course.—Subsequent to the operation there were no convulsions for six months, and during this period the child learned to walk with a few faltering steps. In August 1939 she again began to have epileptiform seizures.

Pathologic Report.—Microscopic examination showed normal brain tissue and foci of gliosis. There was also a small amount of tissue in which glandular

36. Kahn, E. A.: Surgical Treatment of a Pineal Tumor, Arch. Neurol. & Psychiat. **38**:833 (Oct.) 1937.

structures were present. These glandular structures arranged themselves into ducts and acinar forms.

The diagnosis was teratoma.

CASE 12.—*Headache, vomiting and diminution of vision for three weeks, followed rapidly by complete blindness. Patient moribund on admission. Teratoma of midbrain revealed at necropsy.*

A. J., a 19 year old youth, first had headache and vomiting after an injury to his head. His appetite soon became poor. For three weeks prior to his admission to the hospital, on May 22, 1915, he noticed diminution of vision, which soon progressed to complete blindness. Bilateral impairment in hearing had also been progressive for some time. He was admitted to the hospital in a comatose state and soon died.

Necropsy.—Examination of the brain revealed a tumor, measuring 3.5 by 3 cm., involving the midbrain, especially the left optic thalamus and the corpora quadrigemina. The tumor was cystic and greenish yellow and contained areas of old hemorrhage.

Microscopic examination revealed a typical teratoma. Much of the tissue was composed of neuroglia cells and fibers, with numerous hemorrhages. Scattered throughout were islands of cartilage and epithelium. Some of the epithelium forming the wall of very small cavities was columnar in type. Other islands of epithelium had assumed definite tissue patterns to resemble salivary glands and the embryonic acini of the thyroid gland. Tiny areas of squamous epithelium could also be made out. Fat cells, myxomatous tissue and areas of hyalinization were present.

The diagnosis was teratoma.

TERATOMA OF THE SPINAL CANAL

Teratoma and teratoid tumor of the spinal canal are extremely rare. Hosoi,[33] in 1930, found that up to that time only 6 verified cases had been reported. Rasmussen and associates,[31] in 1940, among 557 verified tumors of the spinal cord found only 1 teratoma.

Diagnosis.—This tumor is most frequently associated with some form of spina bifida. The symptoms, like those of epidermoid of the spinal canal, are very slowly progressive. The tumor frequently produces a very large spinal canal by pressure erosion of the pedicles and bodies of the vertebra or by spreading the pedicles. These two features, slow progression and large, often spindle-shaped, enlargement of the lumbosacral portion of the spinal canal, are characteristic of epidermoid, dermoid or teratomatous tumor, but lipoma may give a similar picture.[37]

Report of Cases.—We have seen 2 cases of teratoma of the spinal canal. Since they have been included in a separate report on mixed tumors of the spinal cord,[26] they will not be recorded in detail at this time.

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37. Stookey, B.: Intradural Spinal Lipoma, Arch. Neurol. & Psychiat. **18**:17 (July) 1927.

CASE 13.—*Paresis of the lower limbs and difficulty in controlling urine, of twenty-five years' duration. Diffuse enlargement of lumbar part of spinal canal revealed in roentgenogram. Partial removal of cystic teratoma. Improvement for seven months, then recurrence and progression of symptoms.*

V. R., a 36 year old farmer, was admitted to the University Hospitals in 1939, with a history of weakness in the lower limbs and difficulty in control of urine for twenty-five years, since the age of 13 years. There had been no appreciable progress of symptoms for twenty-three years, but three years before admission spasmodic pains and increasing spasticity in his lower extremities developed, assocated with increasing difficulty in controlling urine and feces and decrease in sexual potency. Examination revealed a dermal fistulous tract over the upper portion of the sacrum, with hair growing from the opening and about it, paresis of the lower extremities, atrophy of the muscles of the legs, decreased tendon reflexes in the lower extremities and decreased sensation below the second sacral segment. Roentgenograms demonstrated diffuse enlargement of the lumbar portion of the spinal canal, with erosion of the pedicles and posterior parts of the bodies of the vertebrae.

Operation.—Through a laminectomy of the lumbar portion of the spine a partly cystic and partly solid tumor mass connected with the dermal sinus was exposed. Roots of the cauda equina were in places so embedded in the wall of the tumor that complete removal of the tumor with preservation of these roots was considered impossible. Fragments of the cyst wall were left along some of the roots. The cyst was approximately 10 cm. long and 4 cm. in diameter.

Pathologic Report.—Microscopically the tumor contained adult fat cells, myxomatous tissue, cartilage, fibrous tissue, brain tissue, glands with goblet cells and squamous epithelium.

The diagnosis was teratoma.

Result.—Temporary improvement took place, but after seven months there were recurrence and progression of symptoms.

CASE 14.—*Spastic involvement of lower limbs since age of 13 months. Improvement after application of traction. Diffuse enlargement of lumbar portion of spinal canal revealed in roentgenogram. Total removal of cystic teratoma. Recovery and relief.*

A. I., a 7 year old boy, was apparently normal until the age of 13 months, when he became unable to straighten his hips. If placed on his back he would cry until turned on his side. A report of the physical examination at that time mentioned an area of hypertrichosis over the lower lumbar portion of the spine, atrophy and spasticity of the lower extremities and absence of knee and ankle jerks. Roentgenograms revealed spina bifida occulta. Traction was applied for four months, after which the child improved and was able to be up and about until 3½ years of age, when pain in his legs and disturbance of gait developed. Traction was again tried, without effect. Laminectomy was then performed for spina bifida occulta. "A heavy cartilagenous band was removed from the center of the bulging dural sac." This was followed by complete relief of complaints until he was 6 years old, or one and one-half years before admission to the University Hospitals, in December 1940, when there was recurrence of his former symptoms. Roentgenograms showed a diffuse fusiform enlargement of the entire lumbar portion of the spinal canal.

Operation (Dec. 18, 1940).—The laminas over the involved portion of the spine were thin ribbons and bent on slight pressure. A cystic tumor, situated

dorsal to the spinal cord and the roots of the cauda equina and extending from the eighth thoracic vertebra to the upper margin of the sacrum, was removed.

Microscopic Examination.—The cyst wall contained connective tissue, stratified squamous epithelium, cartilage, adipose tissue and glandular acini.

The diagnosis was teratoma.

Course.—Recovery has been almost complete.

COMMENT

Intracranial Epidermoid.—In cases 1, 2, 4 and 5 the tumors were extensively calcified. While calcification has been frequently reported in cases of intracranial dermoid, we find only 1 case of epidermoid with calcification recorded in the literature. In none of the aforementioned cases were mesodermal elements observed, which forced us to place them in the dermoid group. Cases 1 and 5 were remarkably similar. In both the symptoms began with hemiparesis in early childhood and progressed slowly. The tumor in case 1, which was finally removed at the age of 18 years, with recovery, and the tumor in case 2, which was discovered at autopsy, after causing the patient's death at the age of 66, were very much the same in size, shape, structure and location. Case 3 illustrates two of the characteristic features of intracerebral epidermoid. The encephalographic appearance was characteristic of an intraventricular epidermoid, and after operation there was aseptic meningitis, which so frequently follows operation on a tumor of this type. In this case, it is assumed that aseptic meningitis caused death, seventeen days after operation.

Case 4, that of a small but densely calcified tumor, illustrates the tendency of an epidermoid to produce mental symptoms, regardless of its location. The tumor in this case proved to be unfavorably located for removal, since operation left the patient with contralateral hemiplegia and painful paresthesia.

Case 6, that of a bilateral intraventricular cholesteatoma, demonstrates that the same bilateral intraventricular tumor that is common in the horse may also occur in man. We can find no previous case reported in man.

Diploic Epidermoid.—The tumors in cases 7 and 8, like most diploic epidermoids reported in the literature, presented the appearance of a relatively asymptomatic mass in the skull. The diagnosis was made by roentgenograms.

Epidermoid of the Spinal Cord.—The tumor in case 9, an epidermoid of the spinal canal and spinal cord, apparently became infected through trauma with the spinal puncture needle when punctures were made in the treatment of meningitis. The infected epidermoid was thought to be an epidural abscess, and laminectomy was performed. An intra-

dural lesion containing pus and cholesterol crystals was found. That we were dealing with an infected epidermoid was not realized until the third drainage operation was performed, more than a year after the first laminectomy. A far removed dermal sinus over the sacrum was then recognized as the continuation, from the site of suppuration, of an epithelium-lined tract.

Dermoid.—The tumor in case 10, the only dermoid in our series, involved the frontal lobes of the cerebrum. Roentgenograms demonstrated calcification, as they so often do in cases of such a tumor. Partial removal was followed by temporary relief. Recurrence is to be expected unless the epithelial lining is all removed.

Intracranial Teratoma.—In case 11, that of a teratoma of the medial part of the left parietal lobe, the tumor was localized by encephalograms. This tumor, unlike most teratomas, was not well circumscribed; in fact, it was impossible to recognize even approximately the periphery of the tumor. Little improvement followed its removal.

In case 12, that of a teratoma in the pineal region, one of the more frequent sites in which this tumor has been found, the patient was admitted in coma and the lesion was discovered at autopsy.

Teratoma in the Spinal Canal.—Cases 13 and 14 illustrate the very slow progression of symptoms due to involvement of the cord or cauda equina by teratoma and their tendency to be associated with some form of spina bifida and, through slow growth, to produce dilatation of a long segment of the spinal canal.

SUMMARY AND CONCLUSIONS

Fourteen cases of epidermoid, dermoid and teratoma of the central nervous system are reported.

The following interesting features of intracranial epidermoid are illustrated by 1 or more of the 6 cases reported: Cure can be affected by surgical removal; operation may be followed by aseptic meningitis; the tumor may be calcified; when it is in the lateral ventricle it produces a characteristic encephalogram, from which one can not only locate the tumor but recognize it as an epidermoid. Bilateral intraventricular cholesteatoma similar to that frequently found in the horse occurs also in the lateral ventricles of man.

One case of epidermoid and 2 of teratomas of the spinal cord and spinal canal are reported; they illustrate the following characteristic features: They are associated with some form of dysraphia; they are slowly progressive lesions of the cord or cauda equina, and they produce, by pressure erosion, dilatation of a long segment of the spinal canal.

PATHOLOGIC CHANGES IN THE CENTRAL NERVOUS SYSTEM IN EXPERIMENTAL ELECTRIC SHOCK

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The introduction by Cerletti and Bini [1] of the electric shock as a method of treatment of functional psychoses again raises the question as to the effect of the electric current on nerve tissue. The literature on this subject is concerned both with the lethal effect of high tension currents on man (Hassin [2]) and with the nonlethal effect of electric shock in animal experiments. There are two publications which should be reviewed in connection with the latter, the one by Morrison, Weeks and Cobb [3] and the other by MacMahon.[4] The first authors were interested mainly in the histopathologic changes in the brain of rabbits, guinea pigs and cats following electric shock of ten seconds' duration, which was produced in four different ways: (1) with an induction coil, (2) with condenser discharge, (3) with alternating current and (4) with direct current. The outstanding histopathologic feature in all four types of experiments was the presence of meningeal and small intracerebral hemorrhages, accompanied by ganglion cell disease and edema of the brain. Seemingly, the tendency to hemorrhage was greatest after the use of alternating current.

The experiments of MacMahon, though primarily concerned with pathologic changes, are valuable for the recorded physiologic observations. As the source of electricity he used a 6 volt battery and an induction coil. In some of the guinea pigs the abdominal and thoracic

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1. Cerletti, U., and Bini, L.: L'elettroshock, Arch. gen. di neurol., psichiat. e psicoanal. **19**:266, 1938.

2. Hassin, G. B.: Changes in the Brain in Accidental Electrocution, J. Nerv. & Ment. Dis. **86**:668, 1937.

3. Morrison, L. R.; Weeks, A., and Cobb, S.: Histopathology of Different Types of Electric Shock on Mammalian Brains, J. Indust. Hyg. **12**:324 and 364, 1923.

4. MacMahon, H. E.: Electric Shock, Am. J. Path. **5**:333, 1929.

cavities were opened and the action of the internal organs was observed during the shock. The heart contracted strongly and remained in systole during the entire period, and for two to three seconds thereafter the ventricles showed a barely visible and constant tremor, followed by definite fibrillation of the ventricles and, finally, by irregular, rather forceful contractions, which continued for about ten seconds. If the vagus nerve was blocked by atropine, there was no change in rate or rhythm. The cardiac irregularities became more pronounced with each additional shock. There occurred, approximately thirty seconds after the interruption of the electric current, a gradual constriction of the blood vessels which led to blanching of the ears, lasting from five to ten minutes. The activity of the abdominal viscera resulted in defecation, micturition and emission. The intra-abdominal pressure was markedly increased; but atropine given previously prevented all these phenomena. Shock was accompanied by deep inspiration, with a powerful contraction of the intercostal muscles and the diaphragm. The respiration returned only several seconds after cessation of the shock.

At a recent meeting of the American Association of Neuropathologists, Alpers and Hughes [5] described intracerebral and meningeal hemorrhages in cats which had been subjected to electric shock treatment. In discussing this paper one of us (A. W.) briefly reported the results of the experiments which are recorded in this paper.

METHODS AND MATERIAL

Since we previously had gained experience with the histopathologic changes in the central nervous system of the rabbit in experiments with insulin and metrazol shock, this animal was again selected. Altogether, 28 rabbits were used. In imitation of the present technic as practiced in the electric shock treatment of psychotic patients, an alternating current of 50 to 60 cycles was employed. The electrodes, with a surface area of 2 sq. cm., were placed in different positions but in general were applied between the eyes and ears, over the temporo-occipital areas. Electrode jelly was used in every case. As indicated by the meters of the apparatus, the voltage of the current vacillated between 60 and 150 and the density between 65 and 300 milliamperes. The current was allowed to pass for from three-tenths to one-half second. These values indicate the lowest possible amounts of current with which a convulsion was induced.

The type of convulsion resembled closely that observed in man: The current induced, without a preceding clonic stage, an immediate tonic phase, lasting from ten to thirty seconds. Most of the animals seemed to be exhausted and extremely fearful on being touched or on hearing noise for at least five minutes after the seizure. In 16 out of 28 animals complete paralysis of the hindlegs ensued. The paralysis involved also the bladder, rectum and lower abdominal musculature and was seen immediately after the completion of a seizure. It occurred at different

5. Alpers, B. J., and Hughes, J.: Changes in the Brain After Electrically Induced Convulsions in Cats, Arch. Neurol. & Psychiat. **47**:385 (March) 1942.

periods of the treatment (table). The paralyzed animals lost their appetite, and within a few days to a week ascending infections of the urinary tract developed, despite the fact that the bladder and rectum were artificially emptied at frequent intervals. All the animals lost weight, even those without any other clinical

Data on Rabbits Subjected to Electric Shock *

Rabbit No.	Average Voltage	Intensity, Ma.	Time of Stimulation, Sec.	Experimental Period, Days	No. of Treatments	Appearance of Paralysis Following Treatment, Days	Survival After Treatment, Days	Histopathologic Changes
4	85	155	0.3	53	13	..	3	Acute hemorrhages at base of brain
6	75	140	0.3	39	9	..	0	Hemorrhages into medulla oblongata and spinal cord
7	92	120	0.5	13	4	1	7	Hemorrhages into meninges and spinal cord
8	90	156	0.3	40	9	8	1	Hemorrhages into meninges, brain and spinal cord
9	85	165	0.3	39	9	5	0	Hemorrhages into meninges and spinal cord
10	95	90	0.5	13	4	4	7	Hemorrhages into spinal cord and meninges; fracture of vertebra
11	80	150	0.3	49	13	6†	1	Organic hemorrhages into meninges
14	135	290	0.3	43	7	..	30	No hemorrhages found
16	80	130	0.3	53	10	..	32	Multiple hemorrhages into spinal cord
17	70	105	0.3	53	10	..	32	No hemorrhages found
18	85	130	0.3	53	10	..	32	No pathologic changes
19	55	75	0.3	13	4	4	5	Hemorrhages into meninges, base of the brain and spinal cord
20	75	120	0.3	13	4	4	5	Meningeal and cerebral hemorrhages
21	105	120	0.3	5	1	1	4	Hemorrhages into meninges and spinal cord
23	65	80	0.3	5	1	1	4	Hemorrhages into base of brain and spinal cord
25	90	140	0.3	5	1	1	4	Hemorrhages in pons, occipital cortex and midbrain
26	40	40	0.3	16	1	1	15	Hemorrhages into spinal cord
27	30	60	0.3	23	6	..	10	Hemorrhages in cerebellar meninges and corpora quadrigemina
28	30	60	0.3	23	6	..	10	Hemorrhages in base of pons
29	50	80	0.3	23	6	..	10	Hemorrhages of meninges and corpora quadrigemina
30	35	55	0.3	23	6	..	10	No hemorrhages found

* Only those experiments were included in this table in which autopsy was performed immediately after death or in which the animals had been killed.

† Paralysis in right hindleg only.

complications. Only 1 animal, which had been paralyzed after the first treatment, recovered gradually from its paralysis.

In addition, 10 adult white rats were subjected to electric shock. One rat received eight treatments within six hours and was allowed to survive for ten days. The remaining 9 rats were treated every other day for two weeks. Two of them were killed on the day following the last treatment, and 7 were allowed to survive for nine days. The electric current was passed for one-tenth second; the voltage vacillated between 10 and 20, and a density of 30 to 50 milliamperes was used.

HISTOLOGIC REPORT

Rabbits.—In the central nervous system of the rabbits the outstanding histopathologic feature was localized hemorrhages into the pia-arachnoid at the base of the brain and over the cerebellum and the spinal cord. They were combined with small pericapillary and perivenous hemorrhages, located mostly in the brain stem and the spinal cord. The structures of the telencephalon and diencephalon were spared, and only occasionally was a hemorrhage seen in the corpora quadrigemina or at the base of the hypothalamus. In the rabbits which lived only five days after the first shock treatment no progressive organization of the areas of hemorrhages was observed. The red blood cells at this stage had lost their staining affinity for aniline dyes, though they still stained well with iron hematoxylin. In the rabbits which had survived for longer periods, up to four weeks, there was organization of hemorrhages, both into the meninges and into the brain and spinal cord. In the meninges a mild proliferation of the pial connective tissue was seen, combined with a mild increase in the number of phagocytic cells. In the brain and spinal cord mild astrocytic proliferation surrounded the hemorrhage. But organization by compound granular corpuscles was seen only in those places in which greater areas of spinal cord tissue had been destroyed, as in the case of the rabbit which had been injured by the fracture of a vertebra. The relative insignificance of reparative phenomena may be explained by the smallness of the hemorrhagic lesion, which did not lead to massive destruction of nerve tissue but resulted mainly in perivascular compression of the surrounding tissue and mild perivenous edema, following infiltration with plasma and transitory disturbance of the blood supply. The ganglion cells in the immediate proximity of the hemorrhages were shrunken and hyperchromatic, for 200 microns removed normal cells were again seen (fig. 1 *B*). In the spinal cord neuronophagia of anterior horn cells was seen, which, however, was not present in the neurons of the nuclei of the brain stem which were affected by hemorrhage.

The source of the hemorrhage was rupture of thinly walled capillaries and veins. Figure 2 illustrates what happened in association with the vascular disturbances which MacMahon had so ably described in his experiments: Apparently, the powerful contraction of the ventricles following cessation of the electric stimulation, with reestablishment of the arterial flow, encountered resistance on the venous side of the circulation, with stasis of the blood in the lungs. This was indicated by cessation of respiration, which returned, but several seconds after termination of the shock. This sudden increase in venous pressure led to rupture of the thin walls of smaller veins. Figure 2 *B* clearly shows

such a rupture of the wall of a spinal meningeal vein. One end of the disrupted wall is curled up and thickened, and the proliferated perivenous connective tissue has closed the ruptured wall.

It should be emphasized that beyond the area of the small hemorrhages no generalized disease of ganglion cells was seen which might have been indicative of damage following the repeated electric shocks. Special

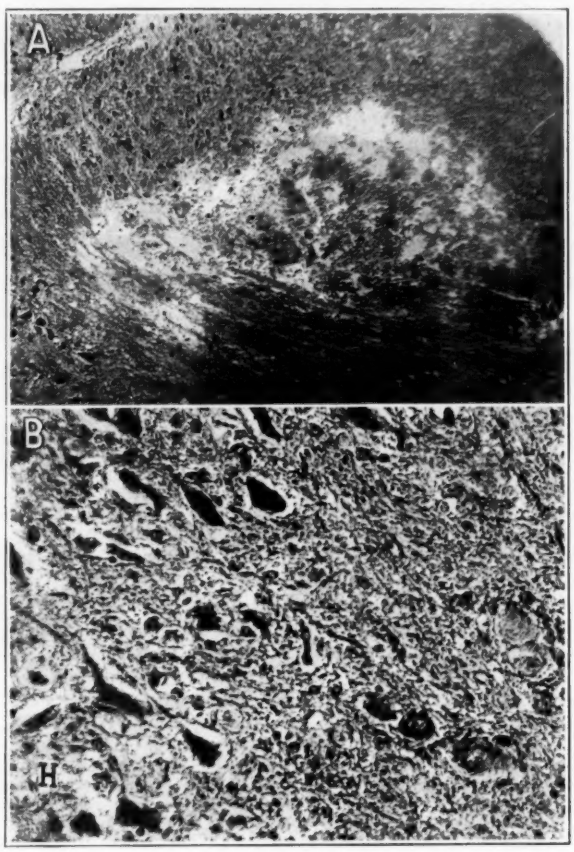

Fig. 1.—*A*, hemorrhage into the superior colliculus of rabbit 25, which received one electric shock and survived the paralysis for four days. The center of intact red blood cells is surrounded by an area of edema, followed in turn by shrunken, hyperchromatic cells. Van Gieson stain; magnification 76.

B, hemorrhage into the medulla oblongata of rabbit 20, which received four electric shocks within eight days, then became paralyzed and was killed four days later. The hemorrhage (*H*) is surrounded by shrunken, hyperchromatic cells, while the neurons at the right lower periphery are normal. Azan stain; magnification 173.

attention was given to the cerebral cortex and the cornu ammonis, which had proved so vulnerable to insulin and metrazol shock treatment. General reactive phenomena of the different types of glia, characteristic of metrazol intoxication, also were absent. In a few brains in which glial proliferation was seen, the change could easily be correlated with the presence of encephalitozoon encephalitis.

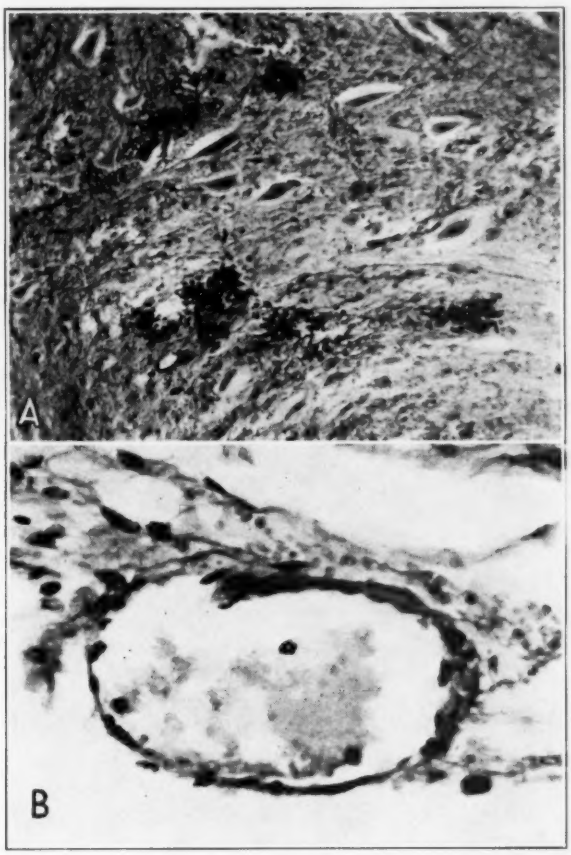

Fig. 2.—Sections from brain of rabbit 9, which received nine treatments during a period of thirty-nine days and became paralyzed on the thirty-first day, after the fifth shock. The animal died after the ninth treatment.

A, longitudinal section of the cervical portion of the spinal cord, showing multiple hemorrhages into the anterior horn with edema, swelling of the myelin sheaths and anemic ganglion cell disease. Weil stain; magnification 173.

B, a ruptured vein within the pia-arachnoid of the posterior portion of the spinal cord. The right end of the ruptured wall is curled and thickened; proliferated connective tissue closes the rupture. Van Gieson stain; magnification 415.

Rats.—In the 2 rats which were killed on the day following the last of seven treatments hemorrhages into the pleura, the lungs and the kidneys could be detected with the naked eye. Microscopically, large areas of the lungs were seen to be congested with blood, which filled most of the alveoli and some of the smaller bronchioles (fig. 4 *A*). In the kidneys the hemorrhages were confined to the cortex and

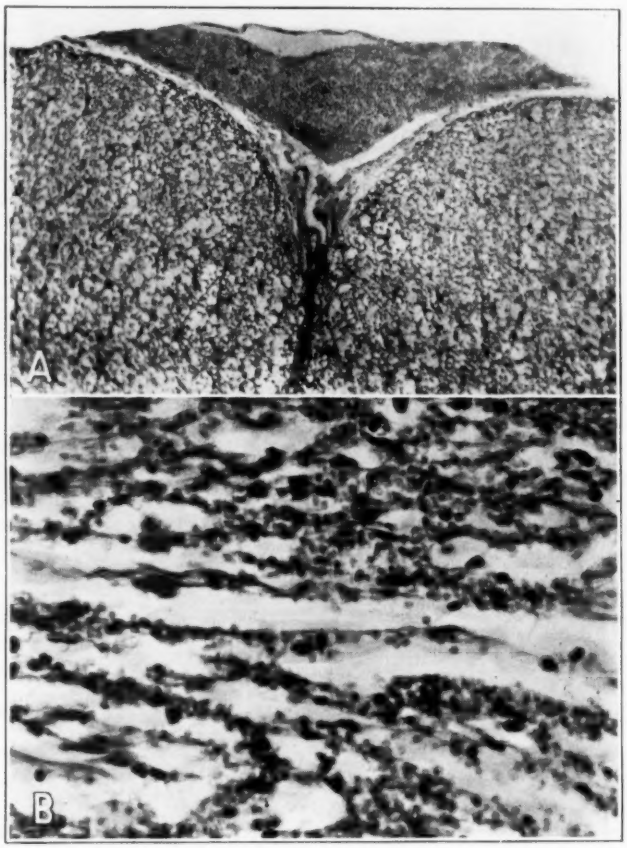

Fig. 3.—*A*, hemorrhage into the pia-arachnoid of the anterior portion of the cervical region of the spinal cord of rabbit 20. Weil stain; magnification 75.

B, hemorrhage into the pia-arachnoid covering the occipital cortex of rabbit 11, which received thirteen electric shocks within forty-eight days and became paralyzed after the fifth, on the thirty-first day. The animal died after the last treatment, two weeks after the paralysis. Swelling and disintegration of the red blood cells and proliferation of fibroblasts and phagocytic cells are evident. Van Gieson stain; magnification 345.

originated from greatly dilated and ruptured veins. In the lungs of the rat which survived the one day treatment for ten days the alveoli were mostly free of fresh blood; however, with higher magnification the shadows of red blood cells could frequently be seen within them. The alveolar septums were thickened and contained an increased number of nuclei, intermingled with some larger scavenger cells (fig. 4*B*).

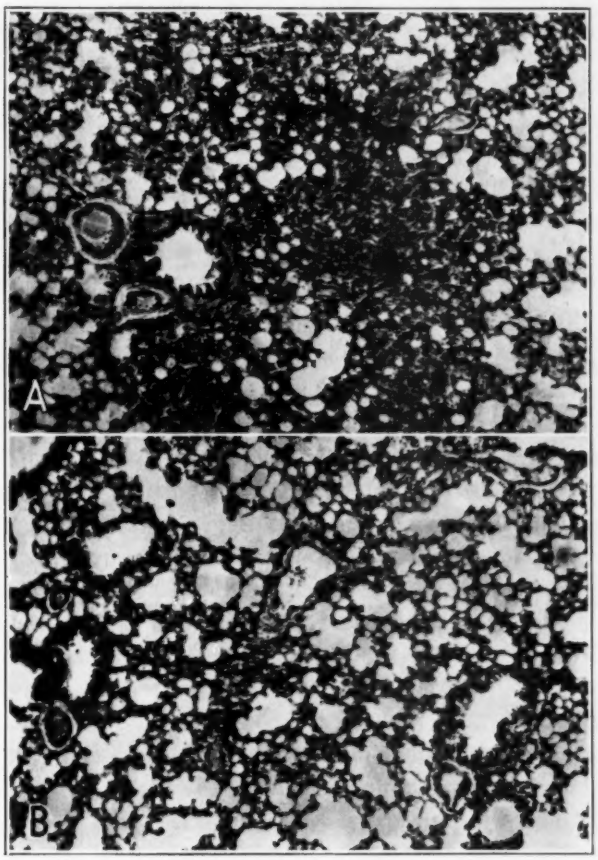

Fig. 4.—*A*, section through the lung of rat 3, which received seven shock treatments during fourteen days and was killed on the day following the last treatment. The alveoli and some of the smaller bronchioles are filled with blood. Van Gieson stain; magnification 55.

B, section through the lung of rabbit 1, which received one electric shock and survived ten days. Shadows of red blood cells are evident in isolated alveoli. The interalveolar septums are thickened and contain an increased number of nuclei, intermingled with larger scavenger cells. Same staining and magnification as in *A*.

These residues of pulmonary hemorrhage were also seen in 3 of those 7 rats which had been treated for fourteen days and had survived for

nine more days. In 2 of them meningeal hemorrhages at the base of the brain were observed; such hemorrhages were also seen in the 2 acute experiments.

COMMENT

In comparing our own results with those of previous investigators there is complete agreement as to the frequency of multiple small hemorrhages within the brain, the spinal cord and their meninges following electric shock. The changes in the myelin sheaths and axis-cylinders, which MacMahon, as well as Morrison and associates, described and which, judging from their reports, appeared to be widespread throughout the brain and spinal cord, were in our experiments confined to the neighborhood of the hemorrhages. Neither did we find the generalized ganglion cell disease which Morrison and associates described as present in the form of "swelling and liquefaction of ganglion cells." They themselves stated, however, that such changes were observed only in induction coil experiments, while with shock produced by alternating current "acute liquefaction of ganglion cells [was] relatively absent." MacMahon had earlier emphasized the fact, which now is generally acknowledged, "that it is difficult to diagnose the early degenerative changes in the ganglion cells . . . because of the variations in size, shape [and] cytoplasmic staining of the cytoplasm and . . . because the nuclei also vary in size, contour, position and staining." In those of our animals in which the contrast of diseased cells with normal cells within the same field was obvious (fig. 1 *B*) or in which satellitosis, or even neuronophagia, was conspicuous, the ganglion cell disease was always confined to the immediate neighborhood of a hemorrhage. As to the histologic changes in other organs, MacMahon remarked that "the pathologic histology in the tissues other than the nervous system is disappointing." He noted congestion of the heart, spleen, kidneys and adrenal glands and periphery of the lobules of the liver and congestion and petechial hemorrhages in the lungs. Microscopically, there were scattered hemorrhages in some skeletal muscles, with degeneration of ruptured muscle fibers. Histologic observations on the lungs and kidneys of our rats, which have already been described, corroborate in general MacMahon's statement.

The question arises whether similar damage might also be produced in man with electric shock treatment. So far no pathologic report has been published, and most observers deny the occurrence of hemorrhages, though occasionally acute subconjunctival hemorrhages have been observed. Examination of the spinal fluid of 10 patients who had been given from one to twelve electric shock treatments showed a negative reaction to the benzidine test and no increase in the cell count. However,

study of the electrocardiogram (Bellet and associates[6]) indicates that the heart is more or less severely affected during the electric shock, as shown by arrhythmia, sinoauricular heart block and other disturbances.

SUMMARY AND CONCLUSIONS

Twenty-eight rabbits and 10 rats were subjected to electric shock treatment simulating the treatment of patients with "functional psychoses."

Sixteen rabbits were paralyzed in the course of this treatment, 7 of them after the first shock. In only 3 of the remaining 12 rabbits was no pathologic change found on microscopic examination. In all the others hemorrhages were present within the meninges of the brain and spinal cord and within the brain stem and the spinal cord. These hemorrhages were usually confined to the immediate neighborhood of capillaries and small veins and were produced by the rupture of the walls of these vessels. A combination of causes was responsible for these ruptures: the sudden rise of the arterial blood pressure during the forceful contraction of the musculature, the vasospasm of the peripheral arteries following cessation of the electric stimulation and the stasis in the venous system, which was aggravated by cessation of respiration for several seconds. Hemorrhages also were present in the lungs of 6 and in the kidneys of 3 out of 10 rats subjected to electric shock.

No generalized ganglion cell disease or generalized proliferative glial reaction was observed. Such phenomena were confined to the immediate proximity of the hemorrhages and were usually combined with a somewhat farther-reaching edema of the surrounding tissues.

DISCUSSION

DR. ARTHUR WEIL, Chicago: It is not the aim of this histopathologic report to pass judgment on the therapeutic effect of a clinical method of treatment. The task of the neuropathologist is to approach as close as possible to this method in his laboratory experiments, to point out the damage done to nerve tissue and to find the minimal dose which may be applied without producing such damage. Within the last four years we have learned through study of the insulin, metrazol and electric shock treatments that, although the clinical manifestations may appear to be similar, the effects on the nervous system of the three methods are entirely different. The irritating effect on the neuron in the case of insulin shock is due to the lack of the important dextrose, producing "intracellular anoxemia." Its pathologic characteristic is a slowly progressing degenerative disease of the neurons. The effect of metrazol is acute, generalized anoxemia, produced by vasoconstriction and followed by intoxication, which results in hypertrophy and hyperplasia of the different types of glia. Electric shock apparently produces

6. Bellet, S.; Kershbaum, A., and Furst, W.: The Electrocardiogram During Electric Shock Treatment, Am. J. M. Sc. **201**:167, 1941.

direct stimulation of the central neurons, followed by reaction of both somatic and autonomic peripheral effectors. The sudden contraction of both the striated and the smooth muscles of arteries and visceral organs leads to shifting of the blood volume, with overflow to the venous system and stasis in the lungs. In addition, there are the cardiac irregularities and the short interruption of respiration following cessation of the electric stimulus.

This stasis on the venous side, together with increased blood pressure, leads to rupture of thin-walled veins and capillaries, for example, within the subarachnoid space and in the lungs.

The danger of electric shock treatment, therefore, lies not in generalized ganglion cell disease but in the possibility of multiple small hemorrhages followed by the process of local repair. That man is not immune to such accidents is shown by the occurrence of subconjunctival hemorrhages. It is to be hoped that by recognizing the limitations and dangers of these three types of shock treatment physicians will learn in the future to apply them selectively to the proper type of functional psychosis, without inflicting too much damage on the nervous system.

DR. JOSEPH A. LUHAN, Chicago: I gathered from the presentation that a neural discharge through the vagus nerve, influencing heart action, may be involved in the pathogenesis of these hemorrhages, and I wonder if Dr. Heilbrunn and Dr. Weil did any work of similar nature on atropinized animals.

DR. NORMAN LEVY, Chicago: The observations reported by Dr. Heilbrunn and Dr. Weil are especially interesting to the clinician. They give a little better understanding of the functional changes in the brains of patients following shock therapy. With Serota and Grinker, I have reported on electroencephalographic disturbances following convulsive shock therapy which lasted for weeks, and in some instances for six or seven months (Electroencephalographic and Clinical Studies Following Metrazol and Electric Convulsive Therapy, ARCH. NEUROL. & PSYCHIAT., this issue, p. 1009). The patients also showed fairly severe clinical evidence of cortical dysfunction. The present report gives some idea of the pathologic basis for these dysfunctions. Unfortunately, we have recently had an opportunity to study the brain of a patient who died of heart failure after an electric shock treatment. The pathologic changes were difficult to evaluate because of the disturbances due to heart failure. There were a considerable number of dilated capillaries with hemorrhages which undoubtedly antedated the acute myocardial failure, as indicated by the presence of blood pigment.

DR. G. B. HASSIN, Chicago: It is strange that in the brains of persons who have been electrocuted legally or accidentally no hemorrhages occur, either in the meninges or in the brain tissues. In only 1 of the 6 cases I have studied was a small hemorrhage observed, and that was in the pons. However, in all 6 cases there were some phenomena which no one had described, in spite of the enormous amount of work done on electrocuted animals.

As the lantern slides show, the brain tissues are broken up into fragments and exhibit rents, tears or fissures. The large blood vessels—the basilar artery and its branches—are broken up. The elastica is separated from the adjacent tunica and is twisted and fragmented; the media is almost divided in two, and the adventitia is thinned. These vascular changes, as well as the cerebral changes referred to, suggest the mechanical action of a strong current, which in cases of electrocution is 2,300 volts and travels from the forehead to one of the lower extremities along the large blood vessels. Why no hemorrhages occur with such powerful currents but do take place in animals I am unable to say.

DR. FREDERICK HILLER, Chicago: There cannot be the least doubt that the pathologic changes are due to circulatory disturbances. The question arises whether the explanation for these disturbances is as simple as the authors think. Are they really due to the combined effect of increased arterial and venous pressures, or does the type of the lesion correspond rather to what Ricker has called prestasis, that is, a vasomotor disturbance within the brain? There is certainly a strong stimulation of the vasomotor system—so strong, in fact, that it might lead to the prestatic phase of Ricker, *Stufengesetz*. The hemorrhages due to diapedesis through capillaries and small veins speak in favor of such an assumption. So does the prevalance of hemorrhage in the meninges, the vessels of which are assumed to be more strongly innervated than the intracerebral vessels. It might be interesting to determine whether hemorrhages occur in the eyegrounds. The detection of such hemorrhages might in some cases permit one to foresee how individual patients will react to this therapy.

DR. L. MEDUNA, Chicago: The observations of Dr. Heilbrunn and Dr. Weil may explain the damage done to the brains of patients by electric shock, although it is improbable that the same pathologic changes are produced therapeutically. The pathologic changes, however, do not explain the beneficial effect of the therapy, and therefore these experiments do not give any information about the mode of action of the electric shock treatment.

DR. VICTOR E. GONDA, Chicago: I have examined the eyegrounds in a number of cases and have never found any hemorrhages, although some of the patients were of advanced age.

DR. CLARENCE NEYMANN, Chicago: Dr. Madden, Dr. Urse and I have treated about 100 patients with electric shock at the Cook County Psychopathic Hospital. Of these, a certain number recovered, at least for the time being; some did not improve. Consequently, Dr. Heilbrunn's and Dr. Weil's clear presentation was especially interesting to us. However, I should like to question them about one point.

They stated that their experiments with animals were similar to the procedure commonly used in treating human beings. Yet they used electrodes with an area of 2 sq. cm. The electrodes generally used for human experiments have an area of about 4 sq. cm. If, therefore, one equates their electrodes in dimensions suitable for human use, considering the relative sizes of the human and the rabbit skull, one would have to use electrodes that were 100 to 200 sq. cm. in area and covered both sides of the head, including most of the neck. The authors used electric currents of 130 volts and 300 milliamperes; such currents would be strong enough to produce electric convulsions in practically any human subject weighing 50 Kg. A rat weighs about 300 Gm.; a rabbit, 2 or 3 Kg. Therefore the analogy of the authors' experiments to the procedure used in treatment of human beings would seem to be questionable. The currents they employed are proportionately much more intense. Owing to the anatomy of the rabbit skull, a much larger part of the current must act on the area near and surrounding the spinal cord than is true when only the frontal regions are in the most direct path of the current. Some of my experiments with rats have shown that with an electrode of less than 0.1 sq. cm. in area convulsions can be produced. Of course, such an experiment is also entirely different from the procedure used in treatment of patients. It is remarkable that no case of serious paralysis has been reported in the literature thus far. Thousands of patients have been treated with electrically induced convulsions. Examination of the spinal fluid after electric shock, as the authors have already stated, has not

demonstrated the presence of blood. At present it is purely conjectural to assume that electric convulsions in human beings are produced by blood stasis, by some effect on the cell groups or by some other means.

There is no question about the anatomopathologic changes which Dr. Heilbrunn and Dr. Weil have demonstrated. However, it is not probable that a solution of this problem will be forthcoming until a careful study has been made of human brains after electric shock therapy. As the current passes through the human brain, most of it travels by the shortest route from one electrode to the other in the form of an arc. Probably most of it passes through the frontal lobes, some back into the posterior parts of the frontal lobes and finally some into the parietal lobes. Dr. Meduna was right in stating that there is always some psychologic effect produced by treatment with electric currents. For this reason, patients were treated with ten subconvulsive shocks; the current had to be reduced to about 30 volts. None of these patients showed any improvement in their behavior or any change in their mental state. They were all much afraid of the treatment because it is very painful, whereas ordinary shock treatments produce no sensation whatever except for a period of amnesia and sometimes a slight headache.

These statements are made without the least criticism of the paper itself, the only purpose being to show the limitations of applying such animal experiments strictly to the treatment of human beings, and thereby of implying that the currents now in common use are destructive to brain tissues.

Dr. Gert Heilbrunn, Chicago: In answer to Dr. Luhan we did not give atropine to any rabbits that were subjected to seizures; such a procedure would have to be the subject of a subsequent study.

We are familiar with Dr. Hassin's work. We looked for the lesions he described but were unable to find them. I agree with Dr. Neymann that both the electrodes and the current used were disproportionately large as compared with those employed with patients. Yet the indicated voltage and amperage were necessary to produce convulsions in the animals. Lower tension and density of the current resulted merely in subconvulsive effects.

It goes without saying that a comparison of lesions and the mechanism of their production in a rabbit brain following electrically induced convulsions with those in a human brain under similar experimental conditions is not feasible. Dr. Levy's observations, however, of hemorrhages in a human brain make at least an implication justifiable.

AN ENCEPHALOGRAPHIC RATIO FOR ESTIMATING VENTRICULAR ENLARGEMENT AND CEREBRAL ATROPHY

WILLIAM A. EVANS JR., M.D.
DETROIT, MICH.

The most frequent encephalographic abnormality in children, and perhaps also in adults, is enlargement of the lateral ventricles. My associates and I have felt the need of a quantitative expression to describe more accurately the degree of enlargement and to define with some precision, if possible, the normal limits of ventricular size. It is assumed, in spite of a few scattered observations reported in the literature to the contrary, that the cerebral ventricles are of a relatively fixed size and shape and, in the absence of disease, do not vary significantly from day to day. Further systematic study is desirable to establish this point. The simplest measurement to make, and at the same time one of the most significant, is the transverse diameter of the anterior horns on a film exposed in the anteroposterior projection with the posterior part of the skull down. This allows filling of the anterior horns when only small amounts of air have entered the ventricular system, and it is in this area, according to our experience, that the most marked changes of generalized cerebral atrophy occur. The outline of the anterior horns is fainter than that of the bodies of the lateral ventricles, and the transverse diameter of the anterior horns is measured somewhat below the level for measurement of the bodies. These measurements often approximate each other in value, but the former is usually a little larger (fig. 1). Davidoff and Dyke [1] have given 3.5 and 4.5 cm. as the limits of normal for the transverse diameter of the bodies of the ventricles (*c-c*, fig. 1). There are lacking, however, an appreciation of the normal variations and, particularly, a standard which would be applicable to the smaller skulls of infants and children. For this purpose it seemed reasonable to borrow the principle of the cardiothoracic ratio and to compute the ratio of the transverse diameter of the anterior horns (*a-a*, fig. 1) to the greatest internal transverse diameter of the skull (*b-b*, fig. 1) viewed in the sagittal direction. This was carried out in

From the Department of Roentgenology, the Children's Hospital of Michigan.

1. Davidoff, L. M., and Dyke, C. G.: The Normal Encephalogram, Philadelphia, Lea & Febiger, 1937.

encephalographic studies made at the Children's Hospital of Michigan during the past seven years, and the results were divided on the basis of the roentgenographic appearance into those for a so-called normal group and those for another group showing varying degrees of ventricular enlargement. Additional measurements were made on a few "normal" encephalograms of adults studied at Harper Hospital.

The figures for the "normal" group, derived from 53 cases, were analyzed, with the following results: The values for the internal diameter of the skull varied from 12.8 to 16.4 cm. The transverse diameters of the anterior horns varied from 2.5 to 4.4 cm., with a mean of 3.4 cm. The standard deviation of these values was ± 0.44 and the coefficient

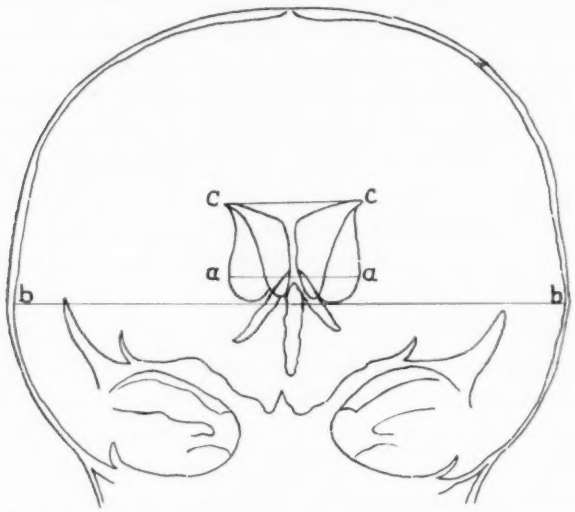

Fig. 1.—Tracing taken from an encephalogram, with the exposure made in the anteroposterior projection and with the posterior part of the head down, showing the measurements which are made. The ratio of the transverse diameter of the anterior horns (*a-a*) to the transverse diameter of the skull (*b-b*) is 3.9:16.5 cm., or 0.24.

of variation 12.9. The values for the ratio of the transverse diameter of the anterior horns to the internal diameter of the skull varied from 0.16 to 0.29, the extreme values being, however, exceptional. The mean value was 0.23, with a standard deviation of ± 0.04 and a coefficient of variation of 0.17. The ratio is thus shown to be a much less variable, and therefore more significant, quantity than the simple measurement of the transverse diameter of the ventricles, as recommended by Davidoff and Dyke.

The results were analyzed in another way by comparing the average values of the ratios for four groups of about equal size with progressively

	Transverse Diameters of the Skulls, Cm.			
	12.8-14.0	14.1-14.7	14.8-15.2	15.3-16.4
No. of cases.....	13	11	15	14
Average ratio.....	0.23	0.24	0.23	0.24

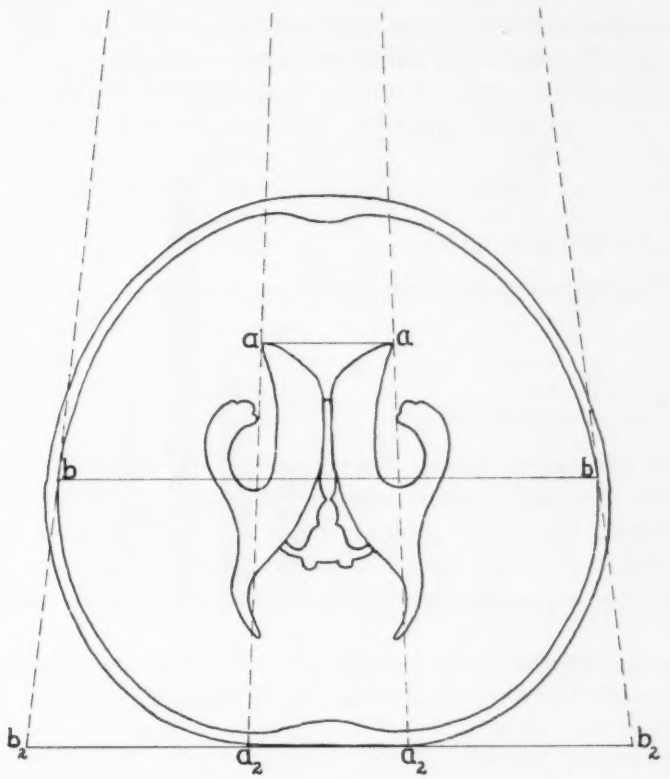

Fig. 2.—Diagrammatic representation of the magnification of measurements used in the encephalographic ratio as the result of projection of the roentgen rays emitted from a point source 76 cm. from the film.

larger skulls. The results indicate that there is no change in the relative size of the ventricles with increasing size of the skull.

A comparison of the average ratio for children and for adults showed no difference (0.23 versus 0.23).

Finally, a computation of Pearson's product moment correlation coefficient, using the values for the internal transverse diameter of the skull and the transverse diameter of the anterior horns, gave a result

of 0.485 (± 0.071), indicating a significant although not close correlation of these values.[2]

The encephalograms were exposed at the standard distance of 30 inches (76 cm.) from the target, which gives an appreciable magnification of objects at any considerable distance from the film. Inasmuch as the anterior horns lie at a different level than the greatest internal transverse diameter of the skull, it seemed advisable to compute the magnification and the ratio for large and small skulls. Ideal examples were used, with the measurements of one skull one third larger than those of the other (fig. 2). Assuming the values in the tabulation,

	Small Skull	Large Skull
a-a	3 cm.	4 cm.
b-b	12 cm.	16 cm.
a-a to plate	9 cm.	12 cm.
b-b to plate	6 cm.	8 cm.
Encephalographic ratio	0.25	0.25

the following results are obtained by computation:

	Small Skull	Large Skull
a_2-a_2	3.402 cm.	4.74 cm.
b_2-b_2	13.02 cm.	17.88 cm.
Encephalographic ratio	0.261	0.265

The calculations indicate that the errors introduced by projection increased the value of the encephalographic ratio by about 6 per cent. The increase was a little greater, but not significantly so, for the large skull than for the small one. For practical purposes, therefore, it seems that one may disregard the effects of projection in making comparative studies.

Another question arises regarding the validity of the normal group. Ideally a normal group would, of course, be composed of a large number of persons free of mental and neurologic symptoms. Because of the discomfort and dangers of the encephalographic procedure, such a selection is impractical. The subjects I have chosen to regard as "normal" were in fact otherwise, for the studies were made because of symptoms which led to a suspicion of damage to the brain. The encephalograms in this group are, then, only relatively normal, and it is likely that a more strictly normal group, if such is ever obtained, would show narrower limits. However, the fact that a significant correlation was obtained between the size of the ventricles and the size of the skull is evidence to support the belief that this group tended to

2. Dr. H. J. Kelly, of the Children's Hospital of Michigan, made the statistical computations, and Miss Emily Cooley prepared the drawings and the tracings of the encephalograms.

be "normal." Davidoff and Dyke suggested that normal variations in the size and shape of skulls and ventricles present insurmountable barriers to significant mensuration, but these did not seem significant in our material, particularly in comparison with the marked pathologic changes that were observed. On the basis of this material we should regard the normal values of the ratio as lying between 0.20 and 0.25. Values between 0.25 and 0.30 indicate early or questionable enlargement, and values above 0.30 signify definite ventricular dilatation.

Large ventricles are seen as the end result of a wide variety of disturbances affecting the brain. The most common are injuries (mechanical or chemical) occurring at the time of birth or later and inflammatory diseases with fever involving the brain, either directly

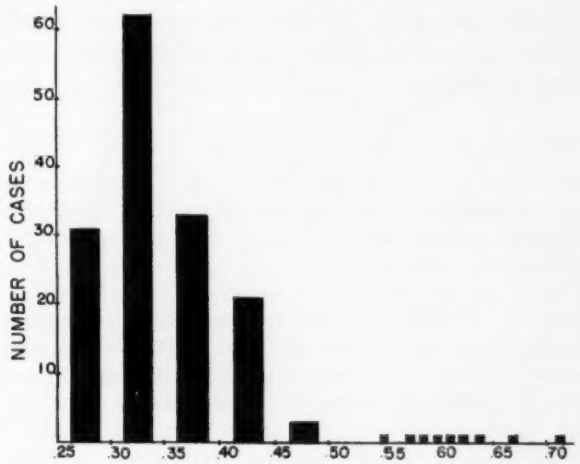

Fig. 3.—Incidence of values obtained for the encephalographic ratio in 159 cases of ventricular enlargement.

(meningoencephalitis) or indirectly, and leading to atrophy of the brain and ventricular enlargement. Less common causes are obstructions by adhesion or tumor in the region of the third or the fourth ventricle. The encephalographic ratio gives a quantitative value for the degree of ventricular enlargement and the extent of the damage to the brain. It is true that other, and occasionally more significant, signs of damage may be present. Variations in the size or symmetry of the skull, enlarged subarachnoid spaces with coarse convolutional markings and blunting of the ventricular contours should also be observed in estimating cerebral atrophy. Abnormal ventricular shapes, such as those associated with agenesis of the corpus callosum and porencephalic cyst, may give better evidence of a brain defect and invalidate ventricular measurements. The ratios obtained in 159 unselected cases in which there was

ventricular enlargement and suitable measurements could be made are given in figure 3, with the incidence of the various values obtained.

In 1 case encephalographic studies were made at an interval of a number of years, and the comparative studies appear to be of value in estimating the progress and prognosis of the condition. In this case of injury to the brain probably occurring at birth, the progressive character of the process is indicated by the rise in the value of the encephalographic ratio, as well as by the gradual aggravation of the patient's symptoms. The value of serial studies following postnatal trauma is shown in an impressive manner in the case reported by King,[3] in which there was a rapid increase in the size of the ventricles following an injury to the head in an 18 month old child, progressing to extreme hydrocephalus and death. The possibility suggests itself that similar observations could be made on the hydrocephalus which follows meningitis to obtain an index of the extent and progress of the damage to the brain and a criterion for the prognosis.

REPORT OF A CASE

A male child, born Oct. 27, 1932 after normal labor, without the use of drugs or instruments, was admitted to the Children's Hospital of Michigan on Feb. 15, 1934. For two weeks he had had a cutaneous rash, with vomiting and a convulsion, accompanied by paralysis of the right arm and leg. Meningitis was suspected, but there was no elevation of temperature and the spinal fluid was normal in all respects. On February 24 a needle was inserted through the anterior fontanel, cerebrospinal fluid removed and air injected. The roentgenograms showed a large accumulation of air in the subarachnoid spaces, especially over the left cerebral hemisphere, indicating advanced cortical atrophy. On March 3 an encephalographic examination was carried out, with removal of 170 cc. of fluid and injection of 160 cc. of air through a spinal puncture needle. The large air-filled sulci were again visualized, and enlargement of both lateral ventricles, with very slight displacement of the ventricular system to the right, was also seen. The diameter of the anterior horns was 5.3 cm. and the transverse diameter of the skull 15.9 cm., giving a ratio of 0.33. On March 7 a bone flap was turned down on the left side, and a quantity of xanthochromic fluid was removed from the subarachnoid space, indicating an old hemorrhage in this area.

Observation at intervals revealed persistent right hemiparesis, with spasticity and shortening of the right achilles tendon, together with mental retardation. The child was readmitted to the hospital on May 13, 1941, with a history of daily convulsions involving the right arm and leg for thirty minutes during the previous two weeks. Encephalographic studies on May 14 showed no air in the subarachnoid spaces of the skull, but there was enlargement of both lateral ventricles and the encephalographic ratio was 6.2:16.1, or 0.39. It was further noted that the left lateral ventricle was a little larger than the right, the ventricular system was displaced slightly to the left and the left petrous ridge slightly elevated as compared with the right.

3. King, G. C.: Encephalography in Rapidly Progressing Cerebral Atrophy Due to Trauma, Am. J. Dis. Child. **56**:1330 (Dec.) 1938.

CONCLUSIONS

The ratio of the transverse diameter of the anterior horns to the internal diameter of the skull as measured on encephalograms (or ventriculograms) exposed in the anteroposterior projection with the posterior part of the head down is proposed as an index of the size of the cerebral ventricles.

The average value of the ratio for a "normal" group was found to be 0.23, with extreme values of 0.16 and 0.29. There is a significant correlation between the size of the ventricles and the size of the skull, and the ratio has the same average value for small and large skulls and for the skulls of infants, children and adults.

The great majority of normal values fall between 0.20 and 0.25; values above 0.30 indicate definite ventricular enlargement and provide a quantitative estimation of the degree of cerebral atrophy.

Serial studies may give an indication of the course of the brain lesion and a basis for prognosis.

10 Peterboro Street.

FATAL INFECTIOUS POLYNEURITIS IN CHILDHOOD

INFECTIOUS NEURONITIS, ACUTE POLYNEURITIS WITH FACIAL DIPLEGIA, GUILLAIN-BARRÉ SYNDROME AND LANDRY'S PARALYSIS

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AND
ALBERT B. SABIN, M.D.
CINCINNATI

Infectious polyneuritis is thought rarely to be fatal in childhood. The usually favorable prognosis of the condition in children has contributed to the impression that the disease is innocuous in the adult as well. That this is not the case is attested to by mortality percentages in adults of from 14 to 42, in series which were studied carefully.[1]

This report is concerned with an instance in which infectious polyneuritis proved to be rapidly fatal in a child. Thorough anatomic and animal inoculation studies were made.

REPORT OF A CASE

A 4½ year old white boy was admitted to the Children's Hospital, Cincinnati, on Nov. 5, 1940. The child had been well except for an attack of whooping cough at the age of 2 years. He had had frequent colds. On October 26 a cold developed which lasted four or five days. On November 1 he complained of pain and weakness in the right lower extremity. On the evening of that day he was unable to turn over in bed. Pain developed in the back of the neck and in the jaws. On the day following he had paralysis of all the extremities and the intercostal muscles. He was able to swallow solid food until November 3, and thereafter he could swallow sips of fluid only. The respiratory embarrassment and dysphagia gradually became worse. He had been brought a distance of 100 miles (16 kilometers) to the Children's Hospital, and on reaching there he had to be placed in a respirator because of the weak respiratory movement and cyanosis.

It was said that there was 1 child with poliomyelitis in the city of the patient's residence at the same time that he was ill. There had been 25 to 35 cases of poliomyelitis in that city during the autumn months.

From the Laboratory of Neuropathology of the Cincinnati General Hospital and the Children's Hospital Research Foundation, and the Departments of Internal Medicine (Neurology) and Pediatrics of the University of Cincinnati College of Medicine.

1. Roseman, E., and Aring, C. D.: Infectious Polyneuritis, Medicine **20**:463-494 (Dec.) 1941.

A complete examination was impossible because the child was in a respirator during the eleven and a half hours that he lived at the hospital. Respirations were labored, with a rate of 18 a minute. He was stuporous on admission, but he responded better after fifteen minutes in the respirator. The temperature was 100 F. and the pulse rate 116. The lips were cyanotic. He was able to talk and to swallow sips of water. The pupils were of equal size and regular in outline, and they reacted promptly to flashlight. There was flaccid paralysis of all the extremities. Further examination was not possible.

He expectorated large amounts of mucus frequently. Three hours after admission the temperature had risen to 102.6 F. and the pulse rate was 120 per minute. Six hours after admission swallowing became impossible. The temperature was 103 F., the pulse rate 136 and the respiratory rate 18. He was unable to talk. His color became dusky. Administration of oxygen was started and stimulants were given. The pulse gradually became weak and irregular. Mucus was aspirated from the mouth repeatedly. Perspiration was profuse. One hour before death the pulse was imperceptible, and there were continuous twitching movements of the lower jaw. The cyanosis increased in intensity, and the boy died eleven and one-half hours after he was admitted to the hospital. The clinical diagnosis was poliomyelitis.

Autopsy.—Autopsy was performed six hours after death. The macroscopic abnormalities were mainly in the lungs. The pink pleural surface of the right lung was spotted with several large dark red areas. Gross section of the right lung revealed dark red, friable areas which had an odor similar to that of stomach contents. Early destruction of the parenchyma had occurred. The mucosa of the right bronchial tree was yellow-pink and covered by a slimy pink material. The left lung was dull red and apparently airless. On gross section the tissue was gray-red, glistening and friable. The mucosa of the left bronchial tree was covered by a yellow-gray, mucopurulent exudate. Microscopic examination of the sections of the lungs resulted in the diagnosis of lobular pneumonia on the right, due to aspiration, and acute bronchitis and lobular pneumonia on the left. There was acute inflammation of the mesenteric and cervical lymph nodes. The other gross abnormalities were congestion and edema of the brain and spinal cord.

Blocks were taken from the cerebral cortex, hypothalamus, midbrain, pons, medulla, spinal cord, cauda equina and cervical and abdominal sympathetic ganglia. Sections were stained with hematoxylin and eosin, eosin and methylene blue, cresyl violet, phosphotungstic acid hematoxylin and the Van Gieson stain and by Bodian's 1 per cent strong protein silver (protargol) method and the myelin sheath technic of Smith and Quigley.

Lesions in the Nervous System.—The main lesions were seen in the spinal cord and its rootlets. In the cauda equina there had occurred swelling and vacuolation of myelin sheaths. Axis-cylinders were fragmented, and in many instances in which the fiber was intact swellings were observed along its course (fig. 1). Diffusely scattered aggregations of lymphocytes and polymorphonuclear leukocytes appeared in the interstitial tissue of the nerves of the cauda equina (fig. 2). There was an increase in neurilemmal nuclei. Comparable changes were observed in the anterior and posterior roots. The nerve fibers were widely separated, probably as a result of edema. Congestion was marked.

The meninges of the spinal cord were normal. The cord showed no cellular infiltration, and the nerve cells were well preserved. The lower segments contained nerve cells in which there was mild chromatolysis.

In the white matter of the cord the myelin sheaths were somewhat vacuolated. The fibers were separated, apparently as a result of edema. The changes in the roots and the few alterations in the cord were more obvious in the lower segments, where glial nuclei appeared to be slightly increased. In the sections of the celiac and superior cervical sympathetic ganglia the neurofibrils appeared better preserved than in the dorsal and ventral spinal roots.

Sections of the brain stem and cerebral cortex revealed marked congestion, some distortion of the nerve cells and swollen oligodendrocytes. No inflammatory reaction was observed in any of the sections of the central nervous system.

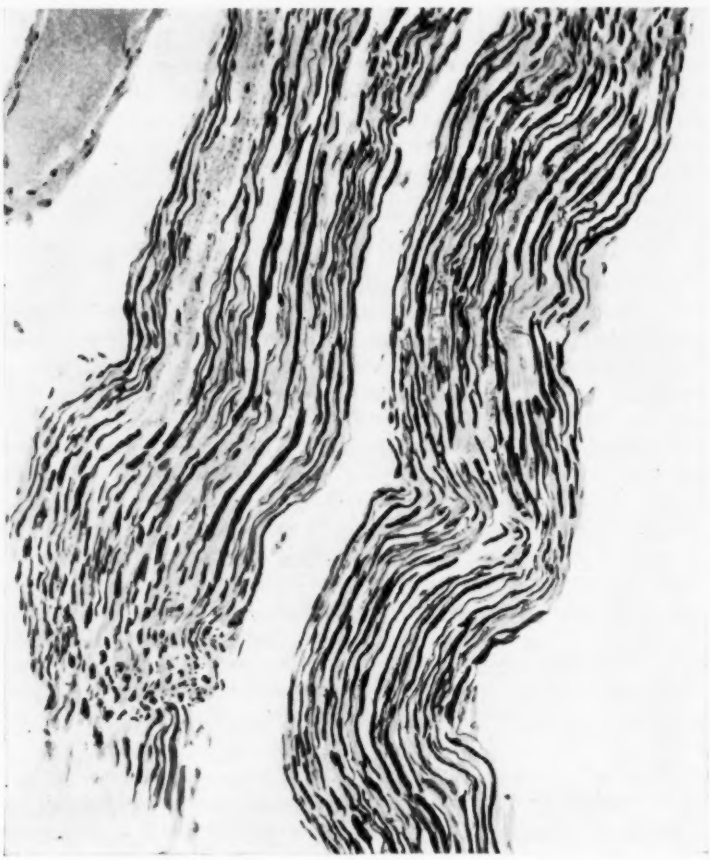

Fig. 1.—Nerves of the cauda equina, showing swelling and disintegration of axis-cylinders. Bodian's strong protein silver (protargol) stain; × 245.

Changes in Other Organs.—A survey of the viscera revealed some of the changes that we have recorded in association with infectious polyneuritis.[2] The heart contained focal areas, suggesting necrosis of isolated muscle fibers. The

2. Sabin, A. B., and Aring, C. D.: Visceral Lesions in Infectious Polyneuritis, Am. J. Path. **17**:469-482, 1941.

majority of the muscle fibers appeared normal with cellular stains, but not infrequently a fiber would tail out into a frayed, homogeneously staining mass, without striation. The appearance of vacuoles along the course of a heart muscle fiber also was not infrequent.

The adrenal glands contained foci of degeneration of cortical cells, usually unaccompanied by cellular infiltration, except for the presence of mononuclear cells in a few of the foci. The liver showed infiltration of the interlobular connective tissue with mononuclear cells.

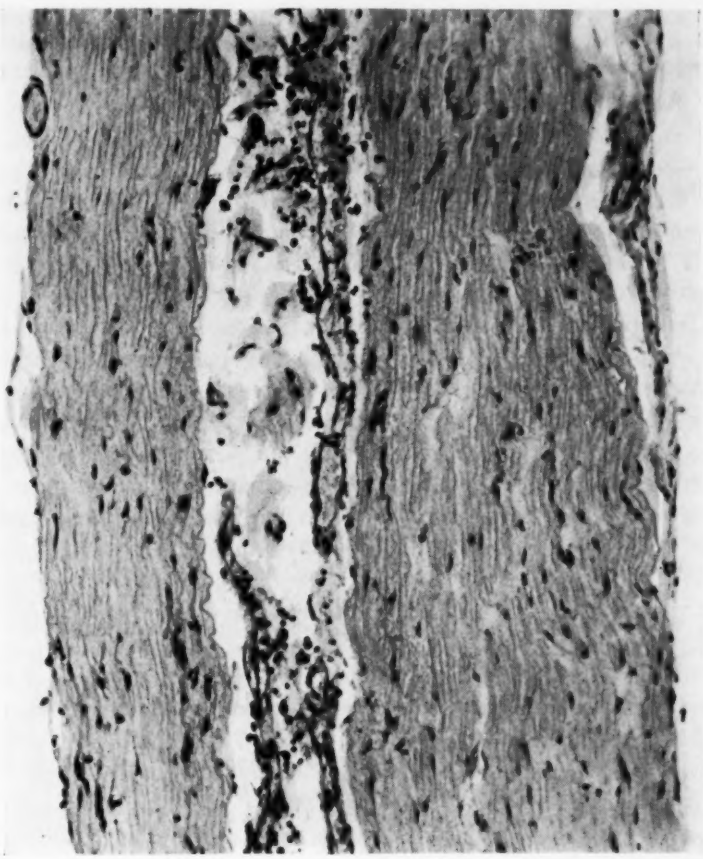

Fig. 2.—Nerve of the cauda equina, showing diffuse infiltration of lymphocytes and polymorphonuclear leukocytes in the interstitial tissue. Eosin and methylene blue; × 163.

Animal Inoculation and Culture Studies.—At the time the necropsy was performed it was believed that we were dealing with a case of poliomyelitis, and consequently 2 rhesus monkeys and 10 mice were inoculated with nerve tissue. One monkey and the 10 mice received a suspension of tissue from the medulla and

pons, both intracerebrally and intraperitoneally, while the other monkey was inoculated with a suspension of the macerated olfactory bulbs. All animals remained well.

A large number of other tissues were obtained at the necropsy, with aseptic precautions, and preserved in the frozen state at the very low temperature maintained by the evaporation of solid carbon dioxide. When the histologic studies indicated that the condition was not poliomyelitis, various tissues were cultured on 30 per cent ascitic fluid agar and the mediums examined at intervals, both macroscopically and microscopically, for ordinary bacteria and micro-organisms of the pleuropneumonia group. Cultures of tissue from the spinal cord, the medulla and pons, the adrenal glands, the liver, the kidneys and the cervical and mesenteric lymph nodes yielded no growth; material from the nasal mucosa, the tonsils and pharyngeal mucosa and the lung yielded staphylococci; a single staphylococcus colony was also present on the plate streaked with the spleen.

COMMENT

The clinical inference that this child had poliomyelitis was quickly disproved by the pathologic examination. The proper diagnosis might have been arrived at clinically had the opportunity for a thorough examination presented itself.

The appearance of the weakness about six days after the onset of, and a day or two after the recovery from, an acute upper respiratory infection is rather common in patients with infectious polyneuritis. Signs of sensory abnormality usually can be elicited in these patients, particularly in the lower extremities. An important diagnostic feature is the usual marked increase in the protein of the cerebrospinal fluid, generally, although perhaps not necessarily, without increase in the cellular content. While it is regrettable that no studies of the cerebrospinal fluid are available in this case, the complete absence post mortem of cellular exudate in the pia-arachnoid suggests that no pleocytosis would have been found.

The toxic changes in the viscera, together with the degeneration of the nerves and the varying degrees of chromatolysis of the nerve cells, establish the diagnosis of infectious polyneuritis. The absence of neuronal necrosis and inflammatory reaction in the central nervous system eliminates poliomyelitis or encephalitis from consideration, a conclusion that is supported by the negative results obtained from the animal inoculations.

Evidently infectious polyneuritis does not always offer a favorable prognosis in childhood. The incidence of fatality in this disease is probably unknown and is likely to remain obscure until careful pathologic studies are made in instances in which children succumb with acute bulbar palsy.

SUMMARY

An instance of fatal infectious polyneuritis in a boy aged 4½ years is recorded. The diagnosis was substantiated by pathologic studies.

FAMILIAL MENTAL DEFICIENCY AKIN TO AMAUROTIC IDIOCY AND GARGOYLISM

AN APPARENTLY NEW TYPE

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THIELLS, N. Y.

There can be little doubt that in the group of so-called familial mental deficiencies numerous types are at present included which actually differ in etiology, clinical manifestations and pathology. Any attempt at singling out clinicopathologic syndromes from this heterogeneous group appears, therefore, of interest. The purpose of this presentation is to describe an apparently new syndrome characterized by severe mental deficiency, peculiar physical signs and conspicuous pathologic changes. The relation of this condition to juvenile amaurotic idiocy and gargoylism will be briefly discussed, and the causation and pathogenesis of the morbid process will be indicated.

REPORT OF CASES

Six cases of this type of mental defect were observed in siblings of one family. The family history included four generations of Italian ancestry on both the paternal and the maternal side. On the paternal line, the grandparents were living and in good health: They had 9 children, 1 of whom died in infancy; the others were living and well and had a total of 16 children (cousins of the patients), who were well both physically and mentally. The father of the patients was of normal intelligence and showed no signs of physical illness; the Wassermann reaction of the blood was negative. On the maternal side the grandfather was in good health, and the grandmother died of a stroke at the age of 68; previous to this she had always had good health and was considered mentally normal. The mother of the patients was living and normal both physically and mentally; she had a negative Wassermann reaction. She had 3 normal sibs, who had a total of 6 normal children.

There was consanguinity in the family: The parents of the patients were cousins, their fathers being brothers.

The sibship consisted of 9 children. The first, a male, was normal both physically and mentally and had 2 normal children. The second and seventh children, both females, were also normal mentally, having graduated from high school, and showed no signs of physical illness. The other 6 sibs were afflicted with the disease. A brief summary of their clinical histories follows:

CASE 1.—M. A., a female, born Sept. 26, 1916, third in the line of birth, was committed to Letchworth Village on Sept. 2, 1925. The patient was a full term baby, born normally after an uneventful gestation. She was breast fed for nine

From the Research Department, Letchworth Village.

months. No feeding difficulties were observed, nor did she ever suffer from any disease except for a slight attack of measles at 2 years of age. Mental deficiency was apparent within the first year of life, the baby showing none of the usual manifestations of early mental activity. Only at 5 years of age could she pronounce a few syllables. Walking was late, the first steps being taken at 4 years of age. Habits of cleanliness were never acquired.

Physical examination on admission showed a well nourished girl whose height was considerably below the normal, being 33 inches (83.8 cm.). This was mainly due to abnormal shortness of the legs. The skull showed no significant deformity; the hair was dry and coarse; the eyebrows were bushy, and there was some growth of hair on the upper lip. The nose was broad, with a deepened bridge, the mouth large and the maxilla prominent. The epiphysial ends of the humerus, femur and tibia were widened, and the lower limbs were bowed. The hands and feet were short and broad. Neurologic examination showed nothing of significance except some increase in the deep reflexes. The Kuhlmann-Binet test showed an intelligence quotient of 13. Routine laboratory examinations of the urine and blood gave normal results.

Nothing of significance occurred during the three years that the patient spent in the institution. Her behavior was that of a hyperactive, low grade idiot. No convulsions were observed, nor did mental deterioration apparently occur.

The patient died Dec. 28, 1928, after a staphylococcic infection which resulted in multiple abscesses of the subcutaneous tissue. Post mortem, the common lesions of diffuse pyemia were observed. In addition, the skull was found to be abnormally thick, being from 1.5 to 2 cm. throughout. The lesser wings of the sphenoid and the orbital plate of the frontal bone were particularly thickened. The brain was not available for histologic examination.

Case 2.—M. J., a male, born May 29, 1917, fourth in the line of birth, was committed to Letchworth Village on Oct. 15, 1930. He was born after a full term, normal pregnancy and weighed 11 pounds (4,989 Gm.). His first year of life was uneventful, physical development appearing normal. During the second year it was noted, however, that he failed to grow in stature and showed marked bowing of the legs. Antirachitic treatment was instituted, without results. At this time it could be definitely ascertained that the child was backward in his mental reactions. At 18 months of age he made some attempts at walking, but progress was very slow and until the age of 10 years his gait was insecure and waddling. He attempted to talk at about 5 years of age, but speech never went beyond a few simple words, pronounced in a guttural voice. He had no illness except for a mild attack of measles and whooping cough in the third year of life. When he was 4 years old bilateral osteotomy was performed to correct the curvature of the legs.

On admission considerable stunting growth was noted, his stature being 42 inches (106.6 cm.), or 15 inches (38 cm.) below normal (fig. 1*A*). He was also 20 pounds (9.1 Kg.) underweight. There was disproportion between the length of the torso and the length of the lower limbs, the legs being shorter than normal. The circumference of the head was within the normal limit (21 inches [53.3 cm.]); the skull was dolichocephalic in type; the hair line was low on the forehead, and the eyebrows were coarse and bushy. The bridge of the nose was large and depressed. The lips were protruding and the jaw appeared well

developed. The neck was short. The hands were short and plump, with slightly tapering finger tips. The tibias were still bowed in spite of the corrective surgical intervention. The feet were broad, flat and short.

No significant alteration of the organs and apparatuses was found at routine physical examination. Neurologically there was increase of the deep reflexes but no other abnormality. The Wassermann reaction both of the blood and of the spinal fluid was negative. There was a slight increase in the protein content of the spinal fluid, but the colloidal gold curve was normal. Psychometric examination at admission showed a mental age of 11 months and an intelligence quotient below 10. A second psychometric examination two years later showed slight improvement, the intelligence quotient being 15, a value which can hardly be considered of significance.

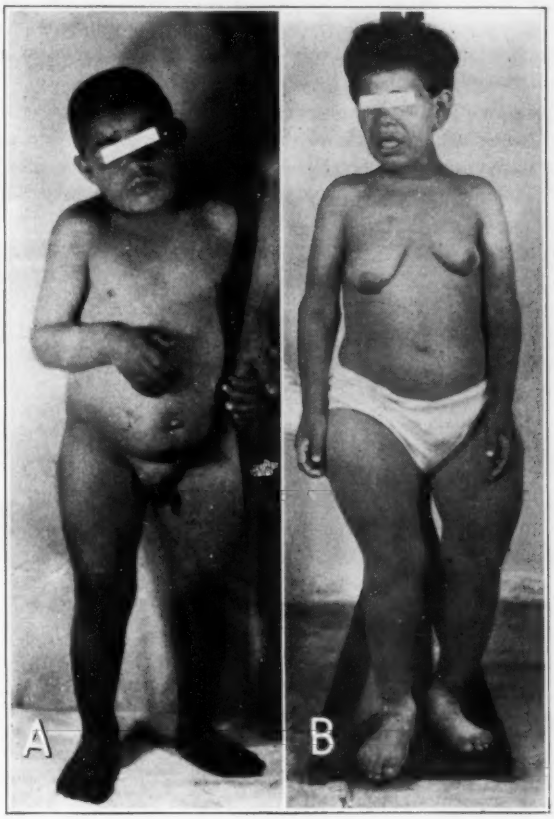

Fig. 1.—*A*, patient 2; *B*, patient 3.

During four years' observation in the institution, nothing significant occurred. In July 1934 a staphylococcic infection of the skin developed, and the patient died of pyemia on September 13. Autopsy was not performed.

CASE 3.—M. A., a girl, born May 13, 1918, fifth in the line of birth, was admitted to Letchworth Village on Oct. 15, 1930. She was a full term baby,

born normally after an uneventful gestation. She was small and delicate and, although no feeding difficulties were experienced, was never well developed or nourished. Mental defect was apparent from an early age. When 5 years old she was committed to an institution. Because of a deformity of the tibias recalling saber shin, she received antisyphilitic treatment, although the Wassermann reaction of the blood had been repeatedly negative.

On admission she appeared well nourished but was considerably below normal in stature (fig. 1 *B*). The characteristic physical features already noted in cases 1 and 2 were present. Laboratory examination showed nothing of significance: The cholesterol, calcium and phosphorus of the blood were within normal limits. The spinal fluid was normal in every respect; determination of the total and lipoid phosphorus gave normal values.

Roentgen examination of the skull (fig. 2 *A*) showed increased thickness of the calvarian bones: The tables of the vault were widely separated, and the diploe was spongy, coarsely trabeculated in places and more opaque than normal. The sphenoid wings and the orbital plates appeared particularly thick and dense.

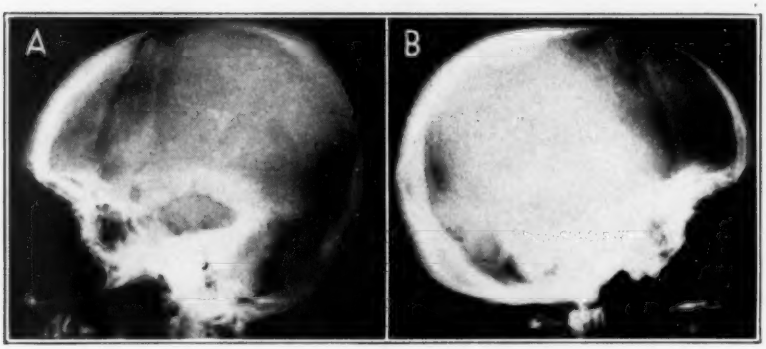

Fig. 2.—Roentgenograms of the skull, showing abnormal thickness and peculiar aspect of the bone. *A*, case 3; *B*, case 5.

In the limbs, in addition to the abnormal shortness and the curvature of the tibias, there was some thickness of the cortex, but no other significant abnormalities.

A psychometric examination showed an intelligence quotient of 19.

During the ten years of residence in the institution no new symptoms appeared. There was no deterioration. Epileptic attacks were never observed. The patient was a hyperactive idiot, emotionally unstable and subject to severe temper tantrums, during which she was unmanageable and destructive.

Case 4.—M. A., a male, born July 28, 1920, was committed to Letchworth Village on Sept. 23, 1931. His history was similar to that of the other affected children in the family. Birth and early physical development appeared normal, but mental defect manifested itself at a very early age by marked retardation of the early manifestations of mental life. He crawled at 2 years of age, attempted to walk only after 3 years and never spoke distinctly. He had no disease of importance. Convulsions were not observed.

On admission he appeared well nourished but considerably undersized, his height being 10 inches (25.4 cm.) below normal. He had the peculiar facies

already described in the other children, the short neck and the stunted limbs. Routine physical examination showed nothing else of significance. Neurologically there was some increase of the deep reflexes but no other abnormality. Psychometric examination, which was performed when the child was 11 years 2 months old, showed a mental age of 2 years 2 months and an intelligence quotient of 10. His behavior in the institution was that of a hyperactive, destructive idiot. Shortly after admission he contracted dysentery, of which he died on Nov. 18, 1931. Permission for autopsy was not granted.

CASE 5.—M. A., a female, born Sept. 28, 1923, eighth in the line of birth, was committed to Letchworth Village on July 26, 1935. She was born of a normal delivery, after an uneventful gestation. The weight at birth was 10 pounds (4,535 Gm.). She was breast fed for fourteen months. There were no feeding difficulties, and the child gained normally in weight. Mental retardation appeared in early infancy: She began to creep only at the age of 18 months, and she could not stand alone until she was 2½ years old; she made no attempt to talk until the age of 6 years; speech had always been limited to a few indistinct, guttural words, with which she expressed her wants. She was in need of constant supervision, being unable to dress or feed herself and unclean in her habits. Since childhood she had been hyperactive and destructive, often exhibiting violent temper tantrums.

On examination at admission she appeared poorly nourished and undersized, her stature being 11 inches (27.9 cm.) below normal. The physical features characteristic of the other affected members were present also in this patient. There was, however, little curvature of the legs. Roentgen examination showed alterations of the skull (fig. 2*B*), essentially similar to those in case 3. Physical examination revealed nothing else of importance. Psychometrically the patient belonged to the idiot group, her intelligence quotient being below 20.

There were no significant changes during the following years. On March 13, 1941, she died of bronchopneumonia.

CASE 6.—M. M., a male, born in 1925, ninth in the line of birth, was never admitted to an institution, nor was any medical record available concerning his condition. According to the parents, his physical features and general behavior were similar to those of the other affected children. At 5 years of age, when he died of acute appendicitis, he was short in stature, showed bowed legs and was probably an idiot, being unable to speak, feed himself, dress or undress. He could not be trained in habits of cleanliness. As in the cases of the other patients, the history was entirely without significance, and the mental retardation appeared at an early age.

PATHOLOGIC EXAMINATION

Only in case 5 was material available for a complete pathologic examination.

Brain.—The brain (fig. 3) appeared small, weighing 980 Gm.; it was considerably atrophic, as evidenced by shrinkage of the convolutions and gaping of the sulci. This atrophy was evenly distributed throughout the cerebral cortex. The pia was thicker than normal and was opaque; there were no adhesions between the meninges and the cerebral cortex. The lateral ventricles were slightly dilated.

Histologic examination of the brain was carried out with the following technics: Nissl's, Bielschowsky's and the hematoxylin and eosin stain for neuron cells; Weil's and Spielmeyer's for myelin sheaths; Bodian's for axis-cylinders;

Ramón y Cajal's and Holzer's for macroglia, and Hortega's for oligodendroglia and microglia. In addition, numerous methods for staining lipoid substances were employed.

Nerve Cells.—The most striking observation was a universally distributed alteration of the neuron cells. Several stages could be seen. In the most advanced stages, as seen in the Nissl preparations (fig. 4), the cellular body was distended, the Nissl granules had disappeared, the cytoplasm consisting of a delicate meshwork, and the nucleus was displaced toward the periphery of the cell, being at times normal in structure and at others shrunken and dark. The apical dendrite

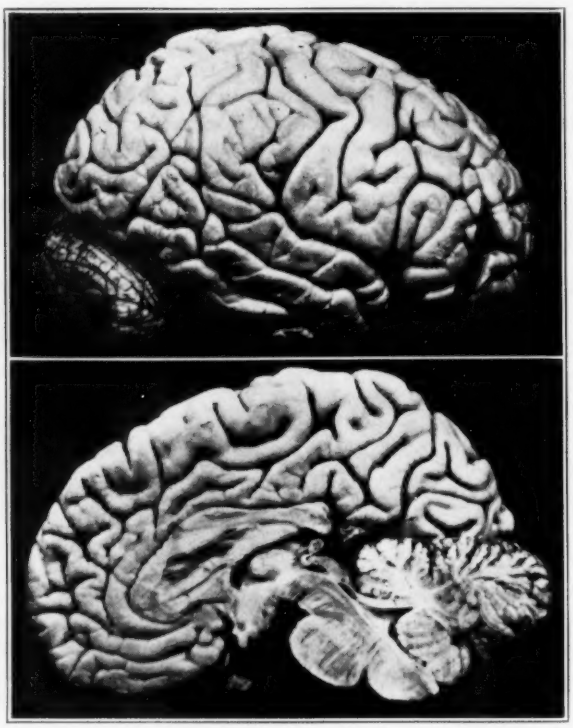

Fig. 3.—External aspect of the brain in case 5, showing generalized atrophy.

of the pyramidal cells showed at times a circumscribed elliptic swelling. In silver preparations (fig. 5) the neurofibrils were collected in clusters near the cellular membrane, while the cytoplasm was occupied by a net of argentophile fibrils, apparently independent of the neurofibrils. In preparations stained by the method for lipids, the swollen nerve cells were filled with small granules which stained mat red or pale orange with scarlet red or sudan III and brownish with sudan black. The Feulgen and Nadi reactions were negative. Osmic acid failed to stain the granules, and with the hematoxylin method of Schaffer, as modified by Hassin, only a brownish tinge was obtained. Nile blue stained the granules deep blue. The material failed to dissolve after remaining several hours in acetone, ether, cold alcohol or cold pyridine; it dissolved slowly in a mixture of hot

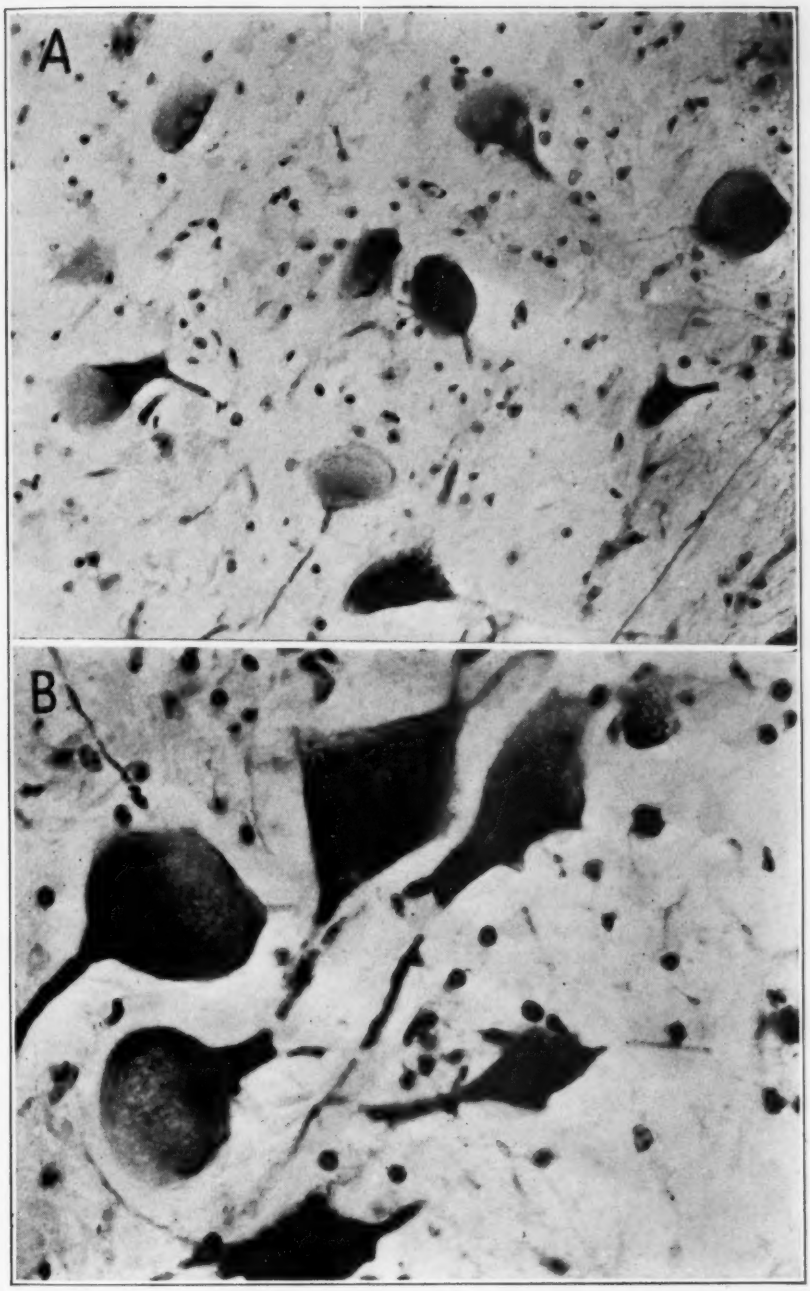

Fig. 4.—Advanced stages of the neurocellular alteration in the Nissl preparation. *A*, magnification 302; *B*, magnification 566.

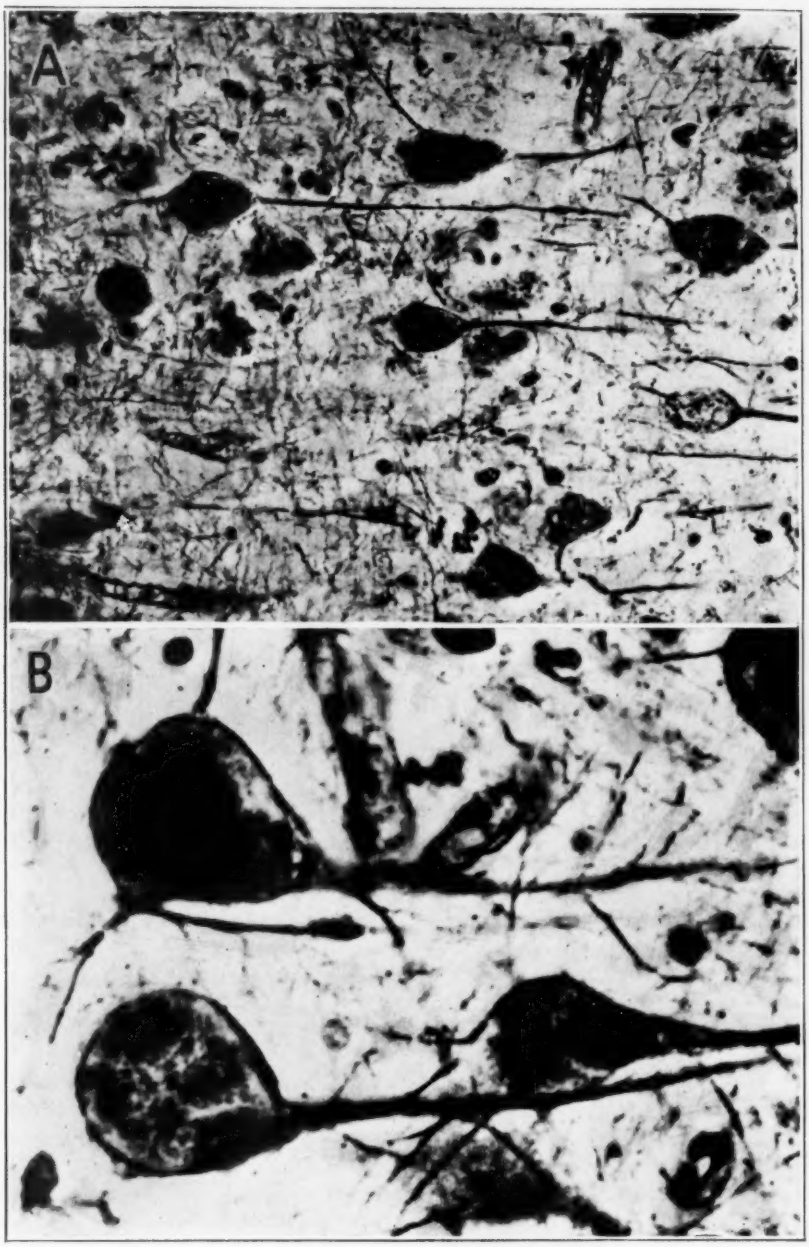

Fig. 5.—Advanced stages of the neurocellular alteration in the Bielschowsky preparation. *A*, magnification 265; *B*, magnification 585.

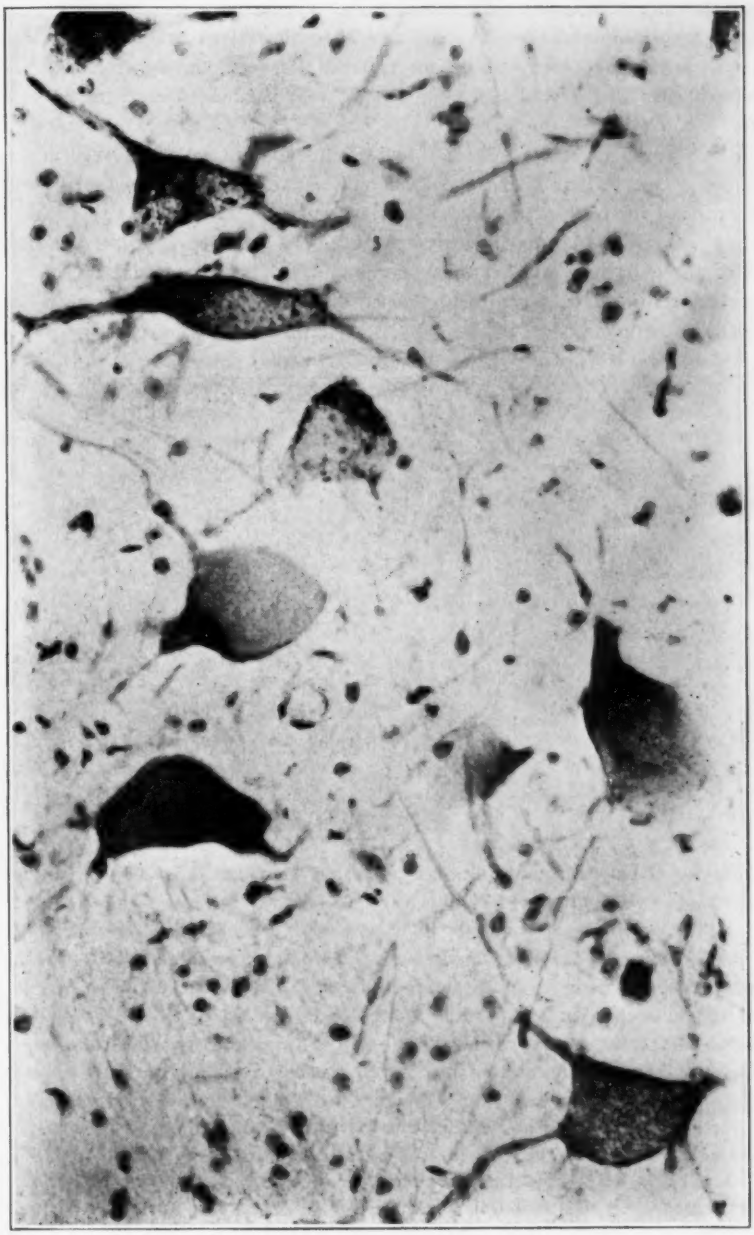

Fig. 6.—Various stages of the neurocellular alteration in the Nissl preparation. Magnification 480.

methyl alcohol and chloroform (3:1) and more rapidly in solutions containing high percentages of acetic acid. During the process of embedding in pyroxylin not all the granules were dissolved and the undissolved material was stained greenish with thionine. Likewise, the material was not entirely dissolved by the xylene in the Bielschowsky procedure and was eventually impregnated by the silver.

In less advanced stages (fig. 6) of the cellular alteration there were moderate swelling of the cell, persistence of a certain number of Nissl bodies, especially those around the nucleus, and eccentric location of the nucleus. At this stage the nucleus was always normal in appearance. Lipoid granules were present in that part of the cytoplasm which was deprived of Nissl bodies. Initial stages of the alteration consisted in the presence of a few lipoid granules within an almost intact cell.

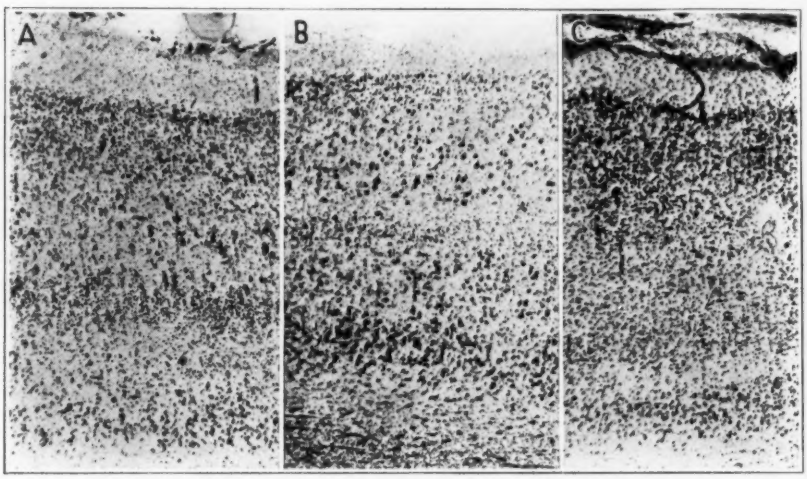

Fig. 7.—Cytoarchitectural alteration in (*A*) area frontalis, (*B*) area temporalis and (*C*) area striata. Magnification 45.

This cellular alteration was ubiquitous; nowhere were there microscopic fields in which cellular changes could not be observed. However, the intensity varied from region to region and within the same region from cell to cell. In the cerebral cortex the large pyramidal cells of the third and fifth layers, as well as the large polygonal cells of the sixth layer, showed frequently advanced changes; actually none of them was spared by the pathologic process. This resulted in some cellular destruction and consequent cytoarchitectural alteration, although the characteristic laminar arrangement was everywhere easily recognizable. Thus, in the frontal lobe (fig. 7 *A*) the third, fifth and sixth layers showed dropping out of nerve cells; in the temporal region the third layer was particularly involved (fig. 7 *B*), while little if any cellular destruction had occurred in the area striata (fig. 7 *C*). In a given microscopic field of the cortex there were to be observed varying stages of cellular change in cells of the same type.

The nerve cells of the striatum were diffusely swollen; however, the large nerve cells were much more involved than the small ones, frequently showing

the most advanced stages of the alteration. A rough estimate of the number of cells revealed that no considerable loss of neurons had taken place in this region. In the thalamus there were severe and diffuse cellular changes; the subthalamic nuclei were also involved, but to a lesser degree. The nerve cells of the nuclei of the third, fourth, sixth, seventh and twelfth nerves were much swollen, while those of the fifth, eighth and tenth nerves were only moderately so. The cells of the pontile nuclei and those of the olives showed little alteration. In the cerebellum, the Purkinje cells contained lipid granules but were only moderately swollen. There was also some dropping out of these cells. This loss, however, was unevenly distributed; some of the folia contained, in fact, a normal number of cells, while others were severely affected. Proliferation of Bergmann glia had taken place in the areas deprived of Purkinje cells. A striking alteration was observed in the molecular layer of the cerebellum: Here the dendrites of the Purkinje cells showed huge, elliptic swellings, which contained granules of material possessing the same solubility and staining properties of the intracellular lipids (fig. 8). In the silver preparations these swellings contained a delicate meshwork of fibrils thinner and paler than the neurofibrils. The number of swellings varied from region to region and was apparently related to the dropping out of Purkinje cells. The granular layer showed no significant changes. Axonal "torpedoes" were not seen.

In the spinal cord the nerve cells showed extensive swelling of moderate degree. The cells of the anterior horn appeared, as a rule, more involved than those of the posterior horn.

Nerve Fibers.—In the Bodian preparations no significant alteration of the axis-cylinders was observed in either the gray or the white matter of the cerebrum; in the cerebellum the various types of fibers were normally present, and in the regions where Purkinje cells had dropped out normal "baskets" could be detected. In the Spielmeyer and Weil preparations no change in myelin sheaths was demonstrable. Only in cortical regions corresponding with the areas of cellular damage was there some apparent decrease of the tangential fibers.

Glia.—In the cerebral cortex the neuroglia cells, as seen in the Nissl, Holzer and Cajal preparations, were increased in number. The increase was everywhere moderate; on closer study of the single glia cells no hypertrophic forms were observed, nor were any lipid granules present within the glial cytoplasm. Similar alterations were seen in the thalamus, while in other regions of the brain no significant changes were observed.

The microglia showed no abnormalities, while the oligogliacytes presented the changes of "acute swelling" diffusely throughout the area examined. The blood vessels had undergone no significant alterations.

Other Viscera.—Particular attention was paid to the study of the spleen and liver. The spleen appeared of normal size and presented no important histologic change. Foamy cells characteristic of lipoidosis were not observed. The liver was enlarged and showed grossly conspicuous fatty changes. On microscopic examination almost every parenchyma cell was observed to contain large cytoplasmic vacuoles, which with specific stains were seen to be filled with fatty material. This stained bright red with scarlet red and was readily dissolved in acetone and ether, thus showing staining and solubility properties differing from those of the lipid infiltrating the nerve cells. Nowhere were foamy cells of the type encountered in lipoidosis observed in the liver.

The endocrine glands presented nothing of significance histologically.

Fig. 8.—Swellings of the dendrites of the Purkinje cells as seen in the Bielschowsky preparation. Magnification 508.

CHEMICAL INVESTIGATIONS

The chemical nature of the lipoid content of the neuron cells was investigated according to the procedure of Klenk.[1] Small pieces of various parts of the central nervous system (dry weight, 34.42 Gm.) were preserved in acetone and successively extracted in a Soxhlet apparatus with acetone (seventy-two hours) and ether (forty-eight hours), then boiled several times with a mixture of methyl alcohol and chloroform (3:1). Three fractions were thus obtained: one, soluble in acetone, consisting of cholesterol and fatty acid; the second, ether soluble, consisting mainly of lecithin and cephalin, and the third, extracted with methyl alcohol and chloroform, consisting of protagon (cerebrosides and sphingomyelins). During the treatment with acetone and ether, some protagon was also extracted, but this separated out immediately from acetone and, on standing twenty-four hours at O C., from ether. This unsoluble fraction was suspended in ether and centrifuged and the precipitate added to the methyl alcohol–chloroform extract, while the supernatant fluid was added to the ether extract. In the acetone extract a small amount of glycerophosphatides was present. The acetone was therefore evaporated, the residuum dissolved in ether, the ether reduced to a small amount

Percentages of Dry Brain Substance Represented by Various Lipoid Fractions

Brain	Cholesterol Fraction	Glycerophosphatide Fraction	Protagon Fraction
Normal (Klenk [1])	8.0	22.9	8.4
Normal (14 year old child; personal case)	12.6	20.8	8.4
Present case	11.0	20.6	11.1
Cases of juvenile amaurotic idiocy (Klenk [1]) (average of 4 cases)	13.2	18.5	11.2

and the ether-soluble phosphatides precipitated with acetone. The residuum from the acetone extract, dried in vacuum, weighed 3.78 Gm. The residuum from the ether extract weighed 7.10 Gm. The residuum from the methyl alcohol–chloroform extract, precipitated with acetone after reduction of the solvent and dried in vacuum to constant weight, weighed 3.84 Gm.

The percentages of dry brain substance represented by these lipid fractions are shown in the accompanying table and are compared with figures obtained for both normal brains and brains of children with amaurotic idiocy of the juvenile type. It will be seen that while the percentages of cholesterol and glycerophosphatides are to be considered normal, the percentage of the protagon fraction was significantly above normal and compares satisfactorily with the figures reported by Klenk [1] in cases of juvenile amaurotic idiocy.

The protagon fraction was further purified, Klenk and Remkamp's [2] procedure being followed in part. The material was dissolved in a warm chloroform–methyl alcohol mixture, and the cerebrosides were crystallized at 0 C. Less than 1 Gm. of lipid was thus obtained, which gave a strong Holisch reaction. The lipids remaining in solution were precipitated with acetone and dissolved in hot methyl alcohol and the impurities precipitated with cadmium acetate. After

1. Klenk, E.: Beiträge zur Chemie der Lipoidosen. Niemann-Picksche Krankheit und amaurotische Idiotie, Ztschr. f. physiol. Chem. **262**:128, 1939.

2. Klenk, E., and Remkamp, F.: Ueber die Reindarstellung von Sphingomyelins aus Gehirn, Ztschr. f. physiol. Chem. **267**:50, 1940.

crystallization from pyridine, the material was dissolved in benzene and alcohol (9:1) and alcohol added until a precipitate was formed. The lipid still dissolved in the benzene-alcohol mixture was precipitated by acetone after reduction of the solvent: A few tenths of a gram was thus obtained, which was made up presumably of sphingomyelin. This lipid was not investigated further. The combined cerebrosides obtained by (*a*) precipitation from the benzene-alcohol mixture and (*b*) precipitation with acetone from the pyridine solution were repeatedly boiled with acetone containing 5 per cent of water, according to the procedure of Klenk;[3] almost half of the material remained unsoluble. As little as 1 mg. of this lipid gave an intense red color when heated with Bial's reagent according to the methods of Blix[4] and Klenk.[3]

COMMENT

Clinical Observations.—The anamnestic data and the clinical manifestations in the 6 cases here reported showed marked similarities. The histories were almost identical in all cases, indicating without exception absence of those "environmental" factors which are usually considered evidence in favor of an exogenous cause of mental deficiency. In fact, there was no apparent disease in the parents; no cases of miscarriage or stillbirth occurred among sibs of the patients; gestation and birth were in every instance normal, and no disease of any importance was noted in any of the patients during growth and development. The physical traits were strikingly similar in all 6 cases, whereas none of the abnormal characteristic features was observed in the normal members of the family. The stature in every case was below the normal. The stunted growth was mainly due to abnormal shortness of the legs, the torso length being nearer normal. The face had a peculiar aspect: It was broad and full; the forehead was narrow, with a low hair line; the eyebrows were coarse and bushy; the bridge of the nose was depressed and enlarged; the nose and mouth were large, and the inferior maxilla was well developed. The hair was abundant, dry and coarse. The skull, dolicocephalic in type, showed no gross deformity. The neck was short, but no anomalies of the cervical vertebrae were noted. There was no deformation of the dorsolumbar portion of the spine; the chest was well formed, and there was no gross enlargement of the abdomen. The limbs were shorter than normal in every case, and the cortex of the long bones appeared thick. In all cases the hands were short and broad; the fingers were also short and clumsy; particularly short was the third phalanx, which had a somewhat clawlike appearance. A slight curvature was noted in the little finger. In all

3. Klenk, E.: Neuraminsäure, das Spaltprodukt eines neuen Gehirnlipoids, Ztschr. f. physiol. Chem. **268**:50, 1941.

4. Blix, G.: Einige Beobachtungen über eine hexosaminhaltige Substanz in der Protagonfraction des Gehirns, Skandinav. Arch. f. Physiol. **80**:46, 1938.

cases there was more or less pronounced curvature of the tibias. Roentgenologic examination showed abnormal thickness of the calvarian bones; the tables were widely separated, and the osseous tissue of the diploe had a peculiar spongy appearance. These changes in the bones were confirmed by postmortem examination in 2 cases.

Examination of the nervous system revealed little of note: There was some increase of the deep reflexes, as is observed often in persons of low grade mentality. There was no motor impairment. Attitudes and movements suggesting involvement of the "extrapyramidal system" were observed, but these are common in idiots. Particular attention was paid to the ophthalmologic examination in 3 cases; the results were without significance. In no instances were epileptic seizures observed.

Mental defect was present in every case and appeared severe, the intelligence quotient being at the idiot level. Symptoms of mental deficiency were noted very early, generally before the end of the first year. No mental deterioration was observed in the 5 patients who were committed to an institution.

Pathologic Observations.—The pathologic changes in the central nervous system observed in case 5 were extremely characteristic, consisting of ubiquitous swelling of the neuron cells and infiltration of the cytoplasm with lipid material. Since the clinical pictures in all 6 cases were almost identical, it is reasonable to assume that a pathologic condition similar to that in case 5 was present also in the other cases. The essential features of the pathologic picture corresponded closely to those in cases of juvenile amaurotic idiocy previously described.[5] However, in the case here reported neurocellular destruction was less conspicuous and glia reaction much less pronounced. Of interest appear to be the cerebellar changes; although the alterations of the Purkinje cells and the granular layer were far less advanced than those observed in the "cerebellar type" of juvenile amaurotic idiocy, the lipid deposits in the molecular layer were extreme.

It has recently been shown that neurocellular changes similar to those encountered in cases of amaurotic idiocy occur also in other conditions. Thus, in a case of gargoylism (Hunter-Hurler syndrome), Tuthill[6] observed diffuse swelling of the cytoplasm of the nerve cells and lipid infiltration; this characteristic pathologic feature of gargoylism

5. Jervis, G. A.: Juvenile Family Amaurotic Idiocy: Its Occurrence in Six Siblings, Am. J. Dis. Child. **61**:327 (Feb.) 1941. Jervis, G. A.; Roizin, L., and English, W. H.: Juvenile Amaurotic Idiocy: Clinico-Pathologic Study of a Case, Psychiatric Quart. **16**:132, 1942.

6. Tuthill, C. R.: Juvenile Amaurotic Idiocy, Arch. Neurol. & Psychiat. **32**:198 (July) 1934.

was confirmed by Ashby and associates [7] and by Kressler and Aegerter.[8] Moreover, in a case of infantile Gaucher's disease, Lindau [9] observed numerous swollen nerve cells containing lipid material which were morphologically identical with those present in amaurotic idiocy. Finally, Norman,[10] in a case of idiocy which in his opinion was different from both amaurotic idiocy and gargoylism, described ubiquitous swelling and lipid infiltration of the nerve cells. In brief, from the case here reported and the data of the literature it would appear that the neurocellular alteration first described in Tay-Sachs disease constitutes a more diffusely distributed type of cellular reaction than is commonly thought.

Differential Diagnosis.—In view of the pathologic similarities of juvenile amaurotic idiocy, gargoylism and the condition in the case described here, it seems pertinent to point out similarities and differences in the salient clinical features of these three types of mental deficiency.

First, mental defect appears at a late period in juvenile amaurotic idiocy, the patients showing normal mental development until the age of 5 or 6 years, when mental deterioration begins and slowly progresses in a period of some ten years to a state of profound idiocy. In gargoylism mental defect is apparent at a very early age and mental deterioration is not the rule, although it has been reported in a few instances (Ellis and associates [11]; Ashby and associates [7]; Henderson [12]; Cockayne [13]). Moreover, a few cases of gargoylism without mental defect have been described (Nonne [14]; Cockayne [15]; Liebenam [16]). In

7. Ashby, W. R.; Stewart, R. M., and Watkin, J. H.: Chondro-Osteo Dystrophy of the Hurler Type (Gargoylism): A Pathologic Study, Brain **60**:149, 1937.

8. Kressler, R. J., and Aegerter, E. E.: Hurler's Syndrome (Gargoylism), J. Pediat. **12**:579, 1938.

9. Lindau, A.: Neuere Auffassungen über die Pathogenese der familiären amaurotischen Idiotie, Acta psychiat. et neurol. **5**:167, 1930.

10. Norman, R. M.: Nerve Cell Swelling of the Juvenile Amaurotic Family Idiocy Type Associated with Tubero-Sclerosis in an Infant Aged Twelve Months, Arch. Dis. Childhood **15**:244, 1940.

11. Ellis, R. W. B.; Sheldon, W., and Capon, N. B.: Gargoylism (Chondro-Osteo-Dystrophy; Corneal Opacities; Hepatosplenomegaly; Mental Deficiency), Quart. J. Med. **29**:119, 1936.

12. Henderson, J. L.: Gargoylism: A Review of the Principal Features with a Report of Five Cases, Arch. Dis. Childhood **15**:201, 1940.

13. Cockayne, E. A.: Hepatosplenomegaly Associated with Mental Deficiency and Bone Changes, Proc. Roy. Soc. Med. **28**:1067, 1934.

14. Nonne, M.: Familiäres Vorkommen (3 Geschwister) einer Kombination von imperfekter Chondrodystrophie mit inperfektem Mixoedema infantile, Deutsche Ztschr. f. Nervenh. **83**:263, 1924.

15. Cockayne, E. A.: Gargoylism (Chondro-Osteo-Dystrophy, Hepatosplenomegaly, Deafness) in Two Brothers, Proc. Roy. Soc. Med. **30**:104, 1936.

16. Liebenam, L.: Beitrag zur Dysostosis multiplex, Ztschr. f. Kinderh. **59**: 91, 1937.

all the present cases profound idiocy had been noted at a very early age and presumably was present at birth. Mental deterioration never occurred. Second, skeletal changes have not been observed in cases of juvenile amaurotic idiocy, while they are integrant features of the clinical picture of gargoylism, in which a variety of cranial malformations and a peculiar alteration of the vertebral bodies, resulting in severe kyphosis and deformity of the limbs, with considerable limitation of the mobility of the joints, are conspicuous. In the present cases cranial malformation and the grotesque facial appearance of persons with gargoylism were not present; there was no kyphosis, and the mobility of the joints was unimpaired. There was, however, abnormal shortness of the limbs, resulting, as in the Hunter-Hurler syndrome, in dwarfism. The peculiar aspect of the bones of the skull bore some similarity to that observed in children with certain blood dyscrasias rather than to the changes observed in persons with gargoylism. Third, in juvenile amaurotic idiocy there is always terminal blindness resulting from atrophy of the optic nerves, often accompanied by pigmentary degeneration of the retina; in gargoylism impairment of vision is also present, owing to multiple opacities scattered throughout the cornea, while in the cases here reported no impairment of vision or pathologic condition of the eyes could be observed. Fourth, enlargement of the liver and spleen occurs in the majority of cases of gargoylism and occasionally is extreme, while this has not been observed in cases of juvenile amaurotic idiocy or in the cases described here. Finally, convulsions are always present in cases of juvenile amaurotic idiocy, whereas they were noted in only 1 instance (Henderson [12]) of gargoylism and never in the present cases.

The question may be raised as to the justification for separating the condition in the cases here described from gargoylism, especially in view of the similarity of the pathologic picture. To be sure, in differentiation of these diseases pathologic data offer no conclusive evidence. For instance, juvenile amaurotic idiocy and gargoylism, although showing a very similar pathologic picture, are undoubtedly distinct clinical entities. Likewise, Tay-Sachs and Niemann-Pick disease, which are almost identical in their neuropathologic features, chemically are distinct types of lipoidosis (Klenk [17]). On the other hand, the disease in the cases described here shows some clinical similarities to incompletely developed gargoylism, such as that described by de Lange and Woltring [18] as "type E." However, the differential symptoms and signs aforementioned appear characteristic enough to justify temporary distinction until more

17. Klenk, E.: Beiträge zur Chemie der Lipoidosen: Ueber einen weiteren Fall von infantiler amaurotischer Idiotie, Ztschr. f. physiol. Chem. **267**:128, 1940; footnote 1.

18. de Lange, C., and Woltring: Der Typus E. Multiple Skelettabartungen, Hepatosplenomegalie, geistige Rückständigkeit, Acta pædiat. **19**:71, 1936.

cases are investigated from the clinical, pathologic and chemical points of view. It is likely that the ultimate distinctive criterion will be offered by the results of the chemical study of the lipids involved in these types of mental defect.

Pathogenesis.—There seems to be a consensus that the presence of intracellular fatty material in cases of both amaurotic family idiocy and gargoylism is evidence of disturbance of lipid metabolism. These conditions are consequently considered forms of lipoidosis. The same conclusion appears justified with respect to the condition in the cases herewith reported. This type of mental deficiency would then constitute a variant of a well known metabolic alteration, of which various forms are presently recognized. As is well known, the chemical constitution of the predominant infiltrating lipid offers a basis for the classification of lipoidosis, three main types being described—cholesterol, cerebroside and phosphatide lipoidosis. It was thought of interest, therefore, to identify the predominant lipid present in the nerve cells in case 5. The staining characteristics of the material were those observed in cases of juvenile amaurotic idiocy and of gargoylism. Staining properties are, however, unreliable means of identification of fatty substances. From the point of view of solubility, the material was characterized by great resistance to common organic solvents: Only in a warm solution containing acetic acid or in a boiling methyl alcohol–chloroform mixture did the lipid dissolve. This observation suggests that the lipid probably belongs to the protagon fraction. Additional evidence was offered by the results of the extraction procedure according to Klenk, as reported in the table. Although, as Klenk [1] himself pointed out, this extraction method gives only relative figures, the amount of the protagon fraction (containing sphingomyelins and cerebrosides) was significantly above normal. Considerable difficulty was experienced in the attempt to purify further this fraction, owing to its small amount. It could be ascertained, however, that the material contained about normal amounts of sphingomyelin and that the quantity of cerebrosides which crystallized out from the protagon fraction dissolved in the chloroform–methyl alcohol mixture was not significantly above normal. These findings suggest that the lipoidosis was neither of the Niemann-Pick type, which is characterized by the presence of large quantities of sphingomyelin, nor of the Gaucher type, in which an abnormally high amount of kerasin is found. The final lipid obtained reacted with Bial's reagent, producing an intense red color. The substance giving this reaction was recently identified by Klenk [3] as an amino acid, "neuramic acid" ($C_{11}H_{21}NO_9$), and found to be a constituent, together with a fatty acid, sphingosine and galactose, of a lipid (so-called substance X) isolated in an abnormally high amount from the brains of patients afflicted with amaurotic familial idiocy. The detection

of this amino acid would indicate that the cases here reported belong from a chemical point of view to the group of "neuramic acid" lipoidoses, which thus far has included only amaurotic idiocy. Further chemical investigations are necessary to establish whether the predominant lipid present in the two diseases is actually identical.

Etiology.—The fact that the type of mental deficiency here described may be included in the group of lipoidoses is of assistance in understanding the etiology of the condition. There is, in fact, strong evidence that in the various types of lipodoses a genetic mechanism is responsible for the occurrence of the metabolic disorder. Sjögren [19] demonstrated that juvenile amaurotic idiocy is genetically determined by an autosomal recessive gene. The available evidence concerning gargoylism suggests that this condition also is inherited as a recessive; in fact, in over half the published cases a familial incidence is shown; moreover, all patients were the offspring of normal parents, and, finally, consanguinity appeared to be more frequent in the affected family than in random samples. The cases here described are too few to permit of a definite conclusion; however, the sudden appearance of an inborn condition affecting several members of a sibship in a family in which no other members are affected and the presence of consanguinity are indicative of a recessive mechanism when, as in the present instances, exogenous factors can be excluded beyond reasonable doubt. One is justified in assuming, therefore, that amaurotic idiocy, gargoylism and the condition in the cases here described have a common cause, being determined by rare recessive genes.

SUMMARY

Six cases of an apparently new type of familial mental deficiency are described. The clinical features consist of severe idiocy, stunted growth, characteristic facies and peculiar changes in the bones of the skull. Pathologically, there is ubiquitous swelling of the nerve cells with cytoplasmic infiltration of lipoid granules.

The relation of this condition to juvenile amaurotic idiocy and gargoylism is discussed. Differences are indicated which appear to justify a separation of this type of mental deficiency. It is pointed out, however, that amaurotic idiocy, gargoylism and the condition in the cases here reported show obvious similarities which warrant their inclusion in the same group of diseases.

The pathogenesis of this condition is discussed, the morbid process being considered an instance of localized lipidosis. From the etiologic aspect, the disease is considered to be genetically determined and, probably, inherited as a recessive.

Miss Miriam N. Swaffield gave technical assistance.

19. Sjögren, T.: Die juvenile amaurotische Idiotie, Hereditas **14**:197, 1931.

ALTERNATING TREMOR AND ITS RELATION TO CORTICAL PATHWAYS

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Within the past few years neurosurgeons have made a concentrated effort to relieve some of the disabilities and deformities in cases of severe paralysis agitans that have not responded to medication. Reports of this work have been published in the 1940 volume of the *Association for Research in Nervous and Mental Diseases, Proceedings.*

In a case of bilateral parkinsonism left hemiplegia followed thrombosis of the right middle cerebral artery. As the patient recovered motor power in the affected extremities it was observed that the tremors present before the hemiplegia did not return. She was observed for the next three years at Montefiore Hospital, and postmortem examination was made at her death. The case is reported in the hope that it may be of help to the neurosurgeon in his attack on this problem. I have been unable to find a similar case in the literature.

REPORT OF A CASE

E. W., a 65 year old white woman, was admitted to Montefiore Hospital on May 5, 1935 with a history of paralysis of the left side of the body, urinary incontinence, occasional frontal and occipital headaches and attacks of blurred vision for eight weeks. For twelve years preceding her admission she had had tremor of both hands, forearms and legs, which began originally in the right arm and then involved the left arm and both legs. There was no history of encephalitis. Two months before admission she awoke at 2 a. m. to find herself paralyzed on the left side, with loss of sphincter control.

Examination.—There was generalized arteriosclerosis, with a blood pressure of 172 systolic and 76 diastolic and an accentuated second aortic sound. The upper lobes of both lungs showed fibrosis. The patient was intelligent, alert and cooperative. There was no defect in her sensorium. When she was first seen, the left arm was held in hemiplegic position and the left leg was dragged and circumducted on walking. A constant rhythmic tremor of small amplitude and a frequency of 5 to 7 per second involved the jaw and the upper and lower extremities on the right side. There was cogwheel rigidity of all extremities, with spasticity of the left upper and lower limbs. The deeper reflexes were active to hyperactive, and extensor plantar responses were present on the left. There was left hypesthesia to pain, temperature and touch sensation. Vibration sense was absent over the entire

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left lower extremity. The left seventh and twelfth cranial nerves showed paresis of supranuclear type. Except for pathologic changes in the electrocardiogram, which indicated an intraventricular conduction defect, the results of laboratory studies were essentially normal.

Course.—The patient remained in the hospital for three years; during this time she improved considerably, so that just before her death she was able to walk about rather freely and could use her left arm considerably in helping herself to dress. There was return of about 60 per cent of motor power in the left extremities. With the return of function no tremors were discernible, even up to the time of her death. The signs of involvement of the pyramidal tract and the sensory changes were unaltered during this period. Severe heart attacks of coronary origin developed, and she died during one of them, on May 12, 1938. A complete postmortem examination was made, and the brain and spinal cord were carefully studied.

Macroscopic Examination of Brain (Dr. Charles Davison).—The brain was small. The vessels at the base showed marked atherosclerotic changes, involving the internal carotid, the anterior and posterior communicating, the basilar and the vertebral arteries. Coronal sections of the brain revealed dilatation of the entire ventricular system, more on the right than on the left. Sections through the beginning of the striatum showed complete destruction of the right caudate nucleus. In sections through the middle of the striatum the following structures seemed to be destroyed completely on the right: the caudate nucleus, the external capsule, the claustrum, the putamen, the pallidum and the internal capsule. Sections through the third ventricle again revealed dilatation of the ventricular system, more on the right than on the left, and destruction of the following structures on the right: the putamen, the caudate nucleus, part of the internal capsule and practically all the pallidal segments. In sections through the substantia nigra, except for shrinkage of this structure, no abnormalities were noted. The following sections were embedded: a complete coronal section through the striatum, a section through the red nucleus and the substantia nigra (for study of myelin sheaths and fat) and sections through the pons, the locus caeruleus and the dentate nucleus and medulla oblongata.

The spinal cord was small and thin but showed no gross abnormalities. One section was taken for the Marchi stain, and another was embedded.

Microscopic Examination of Brain (Dr. Otto Marburg).—Blood Vessels: There was generalized arteriosclerosis throughout the brain, being most pronounced in the region of the striopallidum. Three stages of distinct pathologic change in the walls of the blood vessels could be recognized:

1. Arteriofibrosis. The cells of the intima were swollen but not increased in number; the elastic membrane was thicker than normal and appeared discolored in hematoxylin and eosin preparations, and the media was homogeneous and very thick, as was the adventitia.

2. Atheromatosis. This change was observed only on the affected side, in the arteria cerebri media and its branches to the lenticular nucleus.

3. Calcification. The medium-sized and the smaller arteries in the region of the lenticular nucleus were calcified.

Reaction of the Tissue to Changes in the Blood Vessels: Around vessels presenting arteriofibrotic changes, in the region of the ganglia of the brain stem and in some cortical areas, there were areas of perivascular disintegration. The second and third types of change in the blood vessels were followed by complete destruc-

tion of the surrounding tissue. There were older and younger foci. The older foci consisted of a dense glial cicatrix, with complete disappearance of the nerve tissue; in the younger foci were cystic formations or cribrose states. The spaces in these cribrose states were partly empty and partly filled with compound granular cells and cells that contained hemosiderin. The areas in which some of the blood vessels were filled with granular cells represented the youngest foci and were most ventrolaterally situated. Apparently, the trophic change that produced the foci was at first a sudden, red malacia, and later the process became more chronic and progressive, corresponding to the changes in the blood vessel walls and the destructive influence of these changes on the nutrition of the tissue.

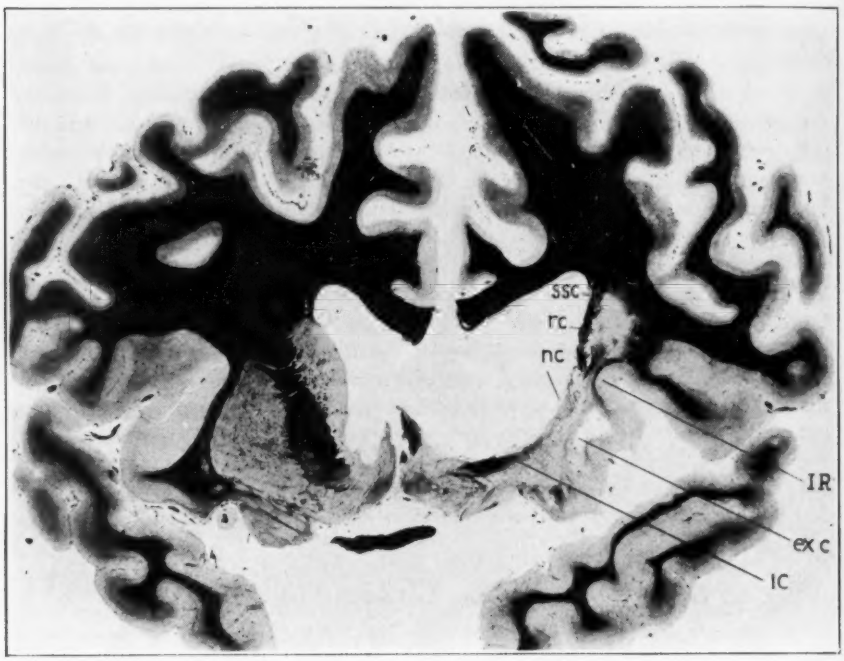

Fig. 1.—Coronal section in the region of the anterior third of the striatum. In this figure, *ex c* indicates external capsule; *i c*, internal capsule; *I R*, island of Reil; *n c*, caudate nucleus; *r c*, reticulated field of the corona radiata, and *s s c*, stratum subcallosum. Weigert-Pal stain for myelin sheaths.

The Foci: 1. A transverse section in the region of the anterior commissure (fig. 1) revealed an enlarged right lateral ventricle with complete disappearance of the head of the caudate nucleus, which was replaced by a small glial cicatrix. The internal capsule had partly disappeared; its most ventral part remained intact; its most dorsal part had completely disappeared, and the intermediate part looked pale and was reduced in volume. In contrast to this severe lesion, the stratum subcallosum was present, though diminished in size, and the reticulated field lateral to it was also present and well developed. A cyst lateral to the reticulated field had destroyed the centrum ovale, between the body of the corpus callosum and

the island of Reil. The neighborhood of the cyst was much lighter in color than the other parts of the centrum ovale. The island of Reil was intact in its dorsal part, while ventrally the capsula extrema was barely evident. Medial to the island, a cyst destroyed the external capsule and the claustrum. Medial to the cyst there was only a bridge of tissue, which represented the lateral boundary of another, dorsally situated cyst, whereas ventrally a cribrose state replaced the entire putamen. Some fibers of the central convolution of the island of Reil were intact. On the left side the caudate and lenticular nuclei, as well as the internal capsule, were intact.

2. A more caudal section through the area of the anterior nucleus of the thalamus (fig. 2) revealed this nucleus to be intact on both sides. The adjacent part of the lateral nucleus of the optic thalamus on the affected side was greatly

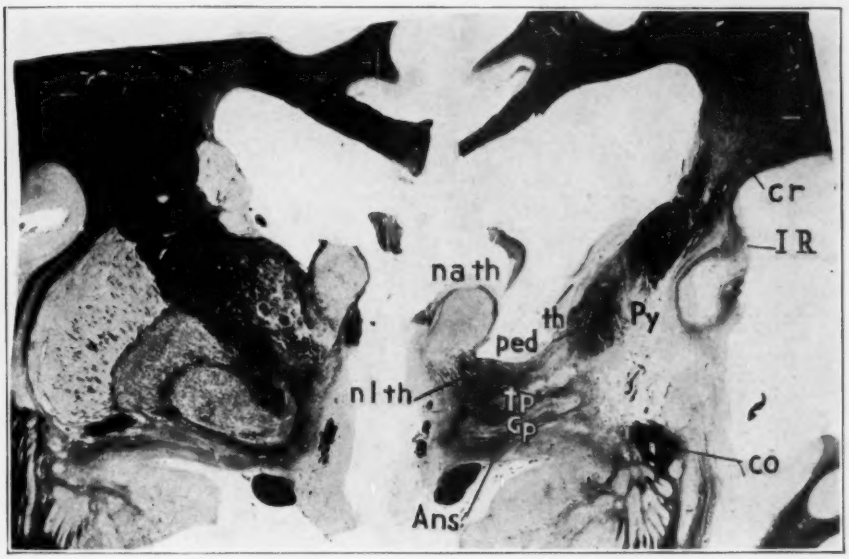

Fig. 2.—Section through the anterior nucleus of the thalamus at a level more caudal than that shown in figure 1. *Ans* indicates ansa peduncularis; *c o*, anterior commissure; *c r*, corona radiata; *g p*, globus pallidus; *I R*, island of Reil; *n a th*, anterior thalamic nucleus; *n l th*, lateral thalamic nucleus; *ped th*, anterosuperior thalamic peduncle; *Py*, pyramidal tract, and *t p*, frontotemporopontile tract. Weigert-Pal stain.

reduced in size and was filled with nerve fibers. Part of these fibers arising from the lateral nucleus surrounded the cicatrix, replacing the caudate nucleus; other fibers ran into the internal capsule. The internal capsule in this region presented three different pictures: The dorsal part of the capsule was almost intact; the ventral part was completely destroyed and replaced by a dense glial cicatrix, and the intermediate part, again, was subdivided into three areas. The most ventral of these areas was made up of fibers that arose from the optic thalamus and were lighter in color than the adjacent area (almost intact fibers); the dorsal area was intact; between the ventral area and the dorsal intact fibers was a dense

glial cicatrix, surrounded by lighter-stained fiber bundles. The capsule as a whole was reduced in size. The stratum subcallosum was intact. Around the stratum reticulatum was the lighter-colored field of the centrum ovale, crossed by the fibers of the corpus callosum which run from here to the lateral surface of the brain. The island of Reil, the claustrum and the external capsule presented the same picture as in the first section. The putamen and the outer limb of the pallidum were destroyed. The ansa lenticularis was present but was reduced in size. The fibers in the anterior commissure and the substantia perforata on this side were fewer than on the healthy side. Lateral to the anterior commissure fibers from the temporal lobe were disrupted by the focus.

3. In a section through the posterior part of the pulvinar, near the posterior commissure (fig. 3), there was no focus of destruction. (Only one section was available for study.) The red nucleus seemed to be intact but was reduced in size. Lateral to this nucleus, within the field of Forel, was a white stripe, indi-

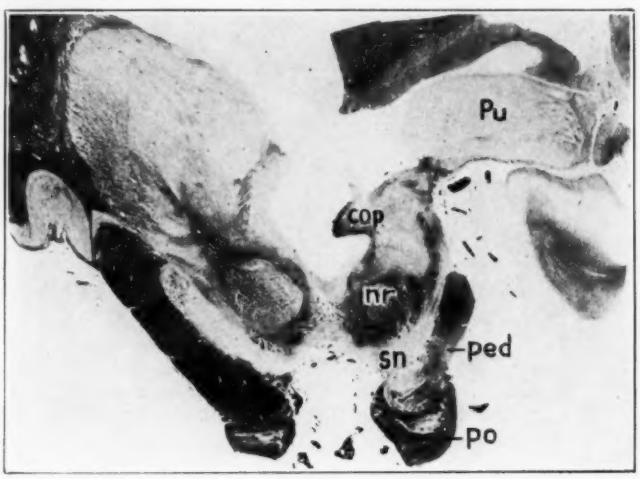

Fig. 3.—Section through the posterior part of the pulvinar. Here, *cop* indicates posterior commissure; *nr*, red nucleus; *ped*, cerebral peduncle; *po*, pons; *Pu*, pulvinar thalami, and *sn*, substantia nigra. Weigert-Pal stain.

cating degeneration of fibers arising from the destroyed areas. The peduncle was one-third the size of that on the normal side. Its lateral part consisted of almost normally stained fibers; its medial part showed only a small amount of fibers, which stained lightly. The field between the two parts was also lighter and smaller than normal. The fasciculus circumligatus was present but atrophic. The pallidopeduncular fibers were present but reduced in number. The stratum intermedium was present medially, whereas laterally there were only a few fibers and these were reduced in size and were lighter than normal. On both sides the substantia nigra was smaller than normal but was rich in cells; on the left side it showed medially a small clear spot, a sign of slight disintegration.

4. A section through the anterior part of the pons (fig. 4) seemed to be entirely normal except that the transversely cut fibers were reduced in size and were light in color. Most affected was the frontopontile system. The temporopontile

system was present but was much lighter in color than that on the normal side. There was generalized reduction in the number of pyramidal fibers. The fibers running from one side to the other were normal except for a few bundles around the

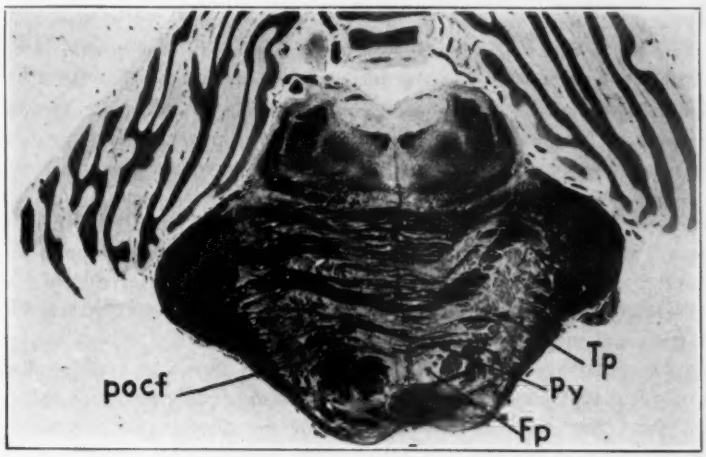

Fig. 4.—Section through the anterior part of the pons. *Fp* indicates frontopontile fibers; *pocf*, pontocerebellar fibers; *Py*, pyramidal tract, and *Tp*, temporopontile fibers. Weigert-Pal stain.

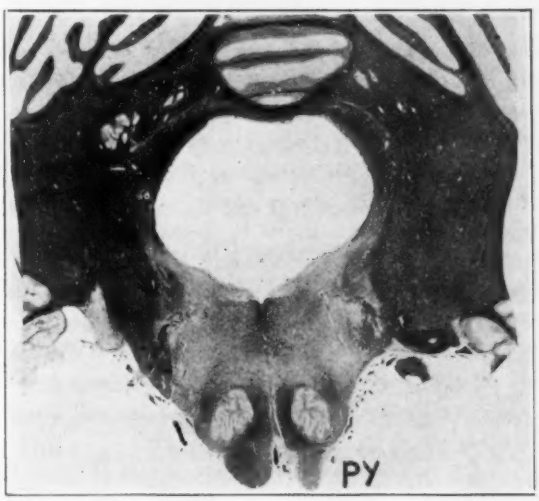

Fig. 5.—Section through the medulla oblongata. The pyramidal tract is indicated by *py*. Weigert-Pal stain.

pyramidal tract of the normal side. The tegmentum pontis presented a difference in the fibers of the fasciculus circumligatus on the two sides.

5. Section through the medulla oblongata (fig. 5) showed that the fibers of the pyramidal tract were reduced to half their normal number.

Secondary Degeneration: The caput nuclei caudati, the putamen and a part of the outer limb of the pallidum were completely destroyed. The anterior limb of the internal capsule, between the nucleus caudatus and the putamen, was also destroyed, as were the genu and the anterior part of the posterior limb. The external capsule, the claustrum, as far as could be seen in the sections available, and a part of the island of Reil appeared to be destroyed. The ventral part of the centrum ovale of the frontal lobe was included in this focus.

Thus, there were secondary degenerations of the frontopontile system as a whole; only a few fibers of this system remained intact. The temporopontile system was better preserved, in spite of the lesion in its anterior part. Because of the site of the focus, I infer that there was also some destruction of the frontothalamic and temporothalamic fibers, since the interior lateral thalamic nucleus was greatly diminished in size and the focus destroyed the temporothalamic radiation. But it should be emphasized that fibers from the anterior thalamic nucleus were present (pedunculus anterior superior). As for the pyramidal tract, the fibers of the genu and most of the anterior part of the posterior limb of the internal capsule were destroyed (fig. 2). Considering the fact that corticothalamic or thalamocortical fibers were to be seen within the degenerated field of the internal capsule, there was no clearcut borderline of the degenerated pyramidal field. Whereas laterally at this level the degeneration seemed to be complete, medially it appeared incomplete. Comparison with the cases of Dejerine revealed the identity of the degenerated field with the fibers of the pyramidal tract. In the region of the peduncle this picture was recognizable only to a lesser degree; in the pons and the medulla there was generalized degeneration, leading to decrease in the size of the tracts (in the medulla to half that on the normal side). It is surprising that, though reduced, the fibers of the stratum subcallosum, as well as the fibers of the reticulated field of the centrum ovale, were present. The destruction of the anterior part of the outer limb of the pallidum must have been the cause of the lesion of the corticolenticular fibers, the existence of which is assumed by some writers. The severity of the damage in the supranuclear rubral system is difficult to determine. The nucleus as a whole seemed to be decreased, and the degenerated stripe in Forel's field, lateral to the nucleus, pointed to the presence of nucleopetal fibers, the origin of which may be the cortex or the subcortical ganglia. The whole peduncular region was smaller than that on the normal side. The substantia nigra had many pigmented cells. The fibers of the stratum intermedium (corticonigral fibers) were absent. Medially the fibers of the fasciculus circumligatus, i. e., the temporopontotegmental system, were present, whereas laterally the frontopontotegmental system was absent; the pallidonigral fibers, though diminished, were present.

In addition, examination of the cerebral cortex showed atrophic changes, particularly shrinking processes, in many ganglion cells on both sides. There were also islands on both sides in which ganglion cells were completely absent. That was true especially of the third layer. It was evident that giant pyramidal cells were present on both sides. Whether these cells were fewer on the affected than on the normal side cannot be decided because the whole of area 4 was not available. In my preparations the cells were seen in the lobulus paracentralis.

COMMENT

There was no primary specific focus in the basal ganglia or in the substantia nigra to explain the presence of the paralysis agitans. Hence one must assume that the disease was caused by profound alterations in the blood vessels throughout the brain, particularly in the brain stem. The results of these vascular alterations were areas of perivascular disintegration, leading to parkinsonism in this case. Since degeneration and disappearance of ganglion cells were to be observed throughout the entire cortex, they cannot be evaluated as the cause of definite clinical signs. Therefore the question arises whether the disappearance of tremor after the insult was due to the degeneration of a definite part of the brain which has some relation to tremor.

In a group of 35 cases of postencephalitic paralysis agitans which were studied at Montefiore Hospital (Davison [1]) pathologically as well as clinically, there were 6 with signs of clinical and pathologic involvement of the pyramidal tract. Yet each of the 6 patients had persistent alternating tremors until the time of his death, regardless of the extent of involvement of the pyramidal system. Tremor may have been reduced, but it was still present. In the case reported here the portion of the pyramidal tract for the leg was relatively intact, though the tremor of the leg disappeared in the same manner as did that of the arm. Some relation of the pyramidal tract to tremor cannot be denied, since three fifths of the tract was destroyed. But other pathways affected by the lesion had their origin in or connections with the frontal lobe; they were:

1. The frontothalamic system. There was evident diminution of the anterior lateral nucleus of the optic thalamus, the connection of which with the frontal lobe, particularly the superior convolution, is well known. The anterior thalamic nucleus and its fibers were intact.

2. The frontopontile and temporopontile pathways. The former was almost completely destroyed; the latter, partially.

3. The corticorubral fibers in Forel's field H, lateral to the red nucleus. The small area occupied by these fibers was degenerated.

4. The frontonigral fibers. This path was affected as a whole.

All the pathways mentioned arise from or have connection with the frontal lobe, not only area 6 but the neighborhood of this area. Assuming that the pyramidal tract plays merely a secondary role in the disappearance of tremor, one must admit, on the basis of changes in this case, that not only area 6 but the parapyramidal area in the frontal portion of the brain is closely related to tremor. Many pathways were affected, the origin of which was the entire superior frontal convolution, as well as

1. Davison, C.: Personal communication to the author.

other frontal convolutions. Thus, it is not sufficient to eliminate area 6 when attempting to destroy all the fiber connections of the superior frontal convolution.

SUMMARY

A case is reported of bilateral paralysis agitans which had been present for twelve years when thrombosis of the right middle cerebral artery developed, with resulting left spastic hemiplegia, from which the patient recovered during the next three years with about 60 per cent of voluntary motor power. The tremor (of paralysis agitans) never returned to the affected extremities, however. The rigidity, previously present, was not altered. Postmortem examination revealed complete destruction of the head of the caudate nucleus, the putamen, part of the globus pallidus and portions of the internal capsule. Three fifths of the pyramidal tract, the whole frontopontile system and a part of the temporopontile system, the frontothalamic fibers to the anterior lateral thalamic nucleus, the corticorubral and the corticonigral fibers were affected.

Drs. Charles Davison, Otto Marburg and Tracy J. Putnam gave help in the preparation of this report.

STUDIES ON THE CORPUS CALLOSUM

III. A CONTRIBUTION TO THE STUDY OF DYSPRAXIA AND APRAXIA FOLLOWING PARTIAL AND COMPLETE SECTION OF THE CORPUS CALLOSUM

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On the basis of the concept of a unilateral cerebral dominance in man, Liepmann [1] postulated that in right-handed persons the left hemisphere, by means of the corpus callosum, exercises a dominating influence on the right hemisphere. Liepmann and Maas [2] concluded that involvement of the anterior portion of the corpus callosum produced "sympathetic" dyspraxia in the subordinate hand. According to Lange,[3] apraxia or dyspraxia occurs most consistently after lesions of the corpus callosum or the gyrus supramarginalis of the dominant hemisphere. The studies of Baldy [4] and Critchley [5] on the syndrome of the anterior cerebral artery tend to substantiate the importance of the corpus callosum in

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From the Department of Medicine, Division of Psychiatry, (Dr. Akelaitis) and the Department of Surgery, Neurological Division (Drs. Risteen, Herren and Van Wagenen), University of Rochester School of Medicine and Dentistry, and the Clinics of the Strong Memorial and Rochester Municipal Hospitals.

1. Liepmann, H.: Die linke Hemisphäre und das Handeln, München. med. Wchnschr. **52**:2322 and 2375, 1905.

2. Liepmann, H., and Maas, O.: Fall von linksseitiger Agraphie und Apraxie bei rechtsseitiger Lähmung, J. f. Psychol. u. Neurol. **10**:214, 1907.

3. Lange, J.: Agnosien und Apraxien, in Bumke, O., and Foerster, O.: Handbuch der Neurologie, Berlin, Julius Springer, 1936, vol. 6, pp. 807-960.

4. Baldy, R.: Les syndromes de l'artère cérébrale antérieure, Thesis, Paris, 1927.

5. Critchley, M.: The Anterior Cerebral Artery and Its Syndromes, Brain **53**:120, 1930.

the performance of purposeful and complex movements in the subordinate hand. Other investigators, such as Dandy,[6] Foerster,[7] Armitage and Meagher [8] and Barré and associates,[9] described cases of surgical section of the corpus callosum or destruction of this commissure by neoplasm in which no evidence of dyspraxia in the subordinate hand was found.

The present paper is an attempt to explain these contradictory observations. To date we have observed 23 epileptic patients in whom the corpus callosum was partially or completely sectioned (Van Wagenen and Herren [10]). Five patients in this group exhibited marked preoperative hemiplegia and were not considered suitable for inclusion in this study. The remaining 18 offered the unique opportunity to study praxis unilaterally and bilaterally in each patient before and after operation.

Elaborate laterality studies were made by Smith and Akelaitis.[11] The dominance of eye, hand and foot was investigated in each patient, and the handedness tendencies of members of the family were utilized whenever possible. Ocular dominance was tested by the methods described by Akelaitis.[12] Handedness and footedness were measured by graduated degrees of preference in unilateral and bilateral activities.

Praxis tests included the study of the ability to handle objects and the execution of spontaneous, imitative and requested movements. Throughout the examination, each hand was first tested separately and

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6. Dandy, W. E.: Changes in Our Conceptions of Localization of Certain Functions in the Brain, Am. J. Physiol, **93**:643, 1930; Congenital Cerebral Cysts of the Cavum Septi Pellucidi (Fifth Ventricle) and Cavum Vergae (Sixth Ventricle), Arch. Neurol. & Psychiat. **25**:44 (Jan.) 1931; Benign Tumors in the Third Ventricle of the Brain: Diagnosis and Treatment, Springfield, Ill., Charles C. Thomas, Publisher, 1933; Operative Experience in Cases of Pineal Tumors, Arch. Surg. **33**:19 (July) 1936.

7. Foerster, O., cited by Lange.[3]

8. Armitage, G., and Meagher, R.: Gliomas of the Corpus Callosum, Ztschr. f. d. ges. Neurol. u. Psychiat. **146**:454, 1933.

9. Barré, J. A.; Kabaker; Pernot and Ledoux: Tumeur du corps calleux (Etude anatomo-clinique d'un cas personnel et remarques sur le syndrome calleux), Rev. neurol. **71**:406, 1939.

10. Van Wagenen, W. P., and Herren, R. Y.: Surgical Division of Commissural Pathways in the Corpus Callosum: Relation to Spread of an Epileptic Attack, Arch. Neurol. & Psychiat. **44**:740 (Oct.) 1940.

11. Smith, K. U., and Akelaitis, A. J.: Studies on the Corpus Callosum: I. Laterality in Behavior and Bilateral Motor Organization in Man Before and After Section of the Corpus Callosum, Arch. Neurol. & Psychiat. **47**:519 (April) 1942.

12. Akelaitis, A. J.: Studies on the Corpus Callosum: II. The Higher Visual Functions in Each Homonymous Field Following Complete Section of the Corpus Callosum, Arch. Neurol. & Psychiat. **45**:188 (May) 1941.

then the two together. The tests employed by Liepmann,[13] Meyer [14] and Wilson [15] were utilized. The suggestion of Grünbaum [16] that disturbances of movement can be elicited more easily by having the patient attempt to carry through different activities in the two hands at the same time was utilized. Usually the patient was required to write with one hand and deal cards with the other hand simultaneously. Constructive praxis was studied by Dr. Frances H. Parsons [17] by means of the Kohs block designs.

REPORT OF CASES

The cases were classified as follows:

Group 1.—Cases in which the motor aspects of the neurologic status were normal before and after operation (cases 1 to 10).

(*a*) Partial section of the corpus callosum (cases 1 to 7).

(*b*) Partial section of the corpus callosum at the first operation and complete section of the corpus callosum subsequently (case 8).

(*c*) Complete section of the corpus callosum (cases 9 and 10).

Group 2.—Cases in which the motor aspects of the neurologic status were normal before operation but evidence of cerebral damage was present postoperatively (cases 11 to 13).

(*a*) Partial section of the corpus callosum (cases 11 and 12).

(*b*) Partial section of the corpus callosum at the first operation and complete section of the corpus callosum subsequently (case 13).

Group 3.—Cases in which evidence of cerebral damage (diffuse or focal) was present before operation (cases 14 to 18).

(*a*) Partial section of the corpus callosum (cases 14 to 15).

(*b*) Complete section of the corpus callosum (cases 16 to 18).

GROUP 1: CASES IN WHICH MOTOR ASPECTS OF THE NEUROLOGIC STATUS WERE NORMAL BEFORE AND AFTER OPERATION

(*a*) *Partial section of the corpus callosum* (7 cases).

CASE 1.—H. K., a white girl aged 16, was admitted to the Strong Memorial Hospital on March 12, 1939. Convulsions began at the age of 3 years, but

13. Liepmann, H.: Kleine Hilfsmittel bei der Untersuchung von Gehirnkranken, Deutsche med. Wchnschr. **31**:1492, 1905.

14. Meyer, A.: Examination for Aphasia, in Muncie, W.: Psychobiology and Psychiatry, St. Louis, C. V. Mosby Company, 1939.

15. Wilson, S. A. K.: A Contribution to the Study of Apraxia with a Review of the Literature, Brain **31**:164, 1908.

16. Grünbaum, A. A.: Aphasie und Motorik, Ztschr. f. d. ges. Neurol. u. Psychiat. **130**:385, 1930.

17. Parsons, F. H.: Psychological Tests of Patients One Year After Section of Corpus Callosum, Psychol. Bull. **37**:498, 1940.

during the past two years they had become increasingly frequent. The patient was intelligent, attractive and sociable and interested in music and literature. She played the piano and the French horn. The results of physical and neurologic examinations were normal. Laterality studies showed a tendency to ambilaterality. As a child she preferred the use of her left hand, but at present she did most tasks with her right hand. If a task should require great strength she used her left hand. She was right footed and right eyed.

Operation.—On March 29, 1939 a right frontoparietal craniotomy was performed, and the body and genu of the corpus callosum were sectioned (fig. 1).

Course.—Convalescence was rather slow, the patient complaining of photophobia as a result of marked dilatation of the pupils, which persisted for two

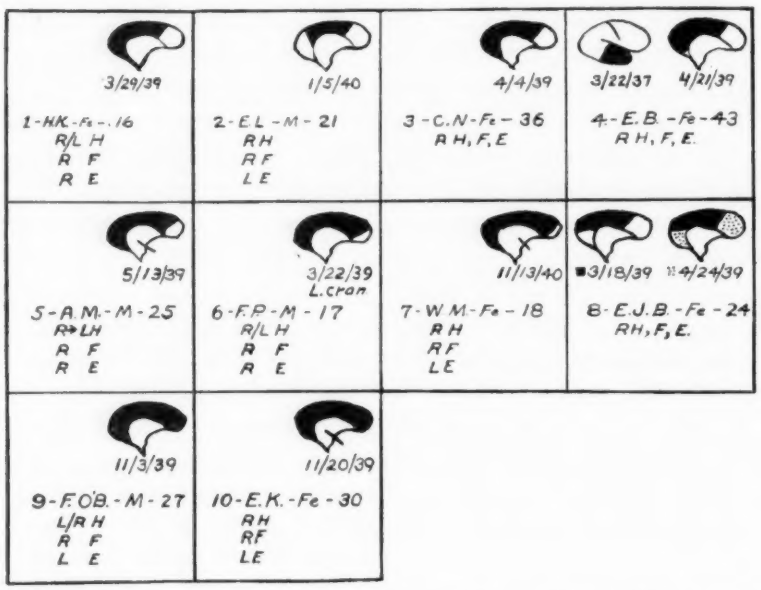

Fig. 1 (group 1; cases 1-10).—Diagrams to illustrate the degree of surgical section of the corpus callosum, as described in the operative notes. The date of operation is given below the individual drawings. In all cases, unless otherwise specified, the craniotomy was performed on the right side. A line through the fornix denotes section of that structure.

In this figure and in figures 2 and 4, *RH* denotes right handedness; *LH*, left handedness; *R/LH*, mixed handedness; *RH→LH*, transfer of handedness from right to left; *RE*, right ocular dominance; *LE*, left ocular dominance; *RF*, right footedness, and *LF*, left footedness.

weeks. For the first two or three days she exhibited weakness and clumsiness of the left hand. This cleared, and subsequently she showed no evidence of dyspraxia in either hand. After discharge, on May 2, she helped around the farm, milking cows and doing housework, and in the opinion of her family, showed no disturbance in these activities. According to the patient and her family, she was able to play the piano and the French horn as well as before

operation. Inasmuch as the seizures returned, she decided to return to the hospital for further treatment. The neurologic status on readmission, June 23, or three months after the first operation, remained normal.

Second Operation.—On July 5, 1939 the right frontoparietal bone flap was reelevated, and during this procedure the patient died. Permission for autopsy could not be obtained. Too rapid intravenous administration of saline solution is suspected of being the cause of death.

CASE 2.—E. L., a white single man aged 22, was admitted to the Rochester Municipal Hospital on Nov. 29, 1939. At the age of 5 years petit mal attacks had developed and at 15, shortly after the death of his father, he began to have grand mal seizures. He was apathetic, superficially intellectual, vague and circumstantial in his talk. The physical and neurologic status was normal. On numerous admissions to the hospital in the past detailed laboratory studies had given essentially normal results. He was predominantly right handed and right footed. Ocular dominance varied with different tests, but most frequently he employed the left eye in sighting.

Operation.—On Jan. 5, 1940 a right frontoparietal craniotomy was performed and the body and posterior half of the genu of the corpus callosum were sectioned. The convolutions of the exposed brain appeared to be atrophic (fig. 1).

Course.—The patient was apathetic and confused for a week after operation. He then began to have frequent grand mal seizures daily, and the apathy became more marked. Sedatives were necessary to control attacks. Throughout this early preoperative period he presented no evidence of dyspraxia in either hand. A detailed praxis study made three weeks after operation revealed no abnormality. After discharge from the hospital, on February 25, he obtained a part time job as maintenance man, and in the early part of October 1940 began to study typewriting in an evening school. After six hours of formal instruction he was able, blindfolded, to type slowly to dictation. Although he made several mistakes, these were merely a result of hitting a key in the immediate neighborhood of the correct key. He always struck correctly that portion of the keyboard intended to be struck with that hand. Since his discharge he has continued to play the piano as well as before operation.

CASE 3.—C. N., a white unmarried woman aged 36, a former school teacher, was admitted to the Strong Memorial Hospital on March 23, 1939. For the past ten years she had been subject to grand mal and petit mal seizures and on several occasions had prolonged psychomotor attacks. She was apprehensive and emotionally unstable, with preoccupations of an idealistic philosophic and abstract religious nature. Physical examination revealed a saccular type of bronchiectasis in the left lung. The neurologic status was normal. Laterality studies showed left cerebral dominance; she was right eyed, right handed and right footed.

Operation.—On April 4, 1939 a right frontoparietal craniotomy was performed and the corpus callosum was sectioned from a point just above the anterior commissure to within 2 cm., more or less, of the tip of the splenium (fig. 1).

Course.—During the first two postoperative days the patient was confused. Several jacksonian seizures involving alternately the left and the right side, without loss of consciousness, were observed. Transient weakness of the left hand was noted. The jacksonian fits quickly subsided. Urinary incontinence, which she feared would be permanent, lasted about a week. This contributed largely to

her depression. A week after operation she showed no dyspraxia in either hand, and the results of neurologic examination were normal. After discharge, on May 3, she was able to play, using both hands, hymns and simple melodies on the piano as efficiently as before operation. She busied herself at canning and sewing and, according to her report and that of her family, showed no evidence of clumsiness in these bimanual tasks. She has been seen on several occasions since her discharge, and the neurologic status remains normal. During the winter of 1930-1940 she studied typing, mimeographing and the use of business machines and, according to her instructors, showed average ability at these tasks.

Case 4.—E. B., a white unmarried woman aged 43, a former secretary, was admitted to the Strong Memorial Hospital on April 17, 1939. Shortly after an unhappy love affair six years before, grand mal, petit mal and "hysterical" attacks developed. In 1937 the anterior two thirds of the right temporal lobe lateral to the ventricle was resected because of a fibrillary astrocytoma. During the past two years she had assumed an invalid role. Physical and neurologic examination, including careful studies of the visual fields, revealed normal status. She was definitely right eyed, right handed and right footed.

Operation.—On April 21 a right frontoparietal craniotomy was performed and the genu, with the exception of a few fibers in its most inferior portion, and the body of the corpus callosum back to the point where the fornix joins it were sectioned (fig. 1).

Course.—The patient convalesced rapidly and two days after operation was found reading and doing cross word puzzles. She did not show any evidence of dyspraxia in either hand during her stay in the hospital. Two days after operation she was able to write with either hand. Since her discharge from the hospital, on May 7, she has faithfully sent a monthly typewritten letter of her progress, enumerating her social activities and the number of attacks she has had. She has continued to live with simple routine. On several occasions she has been examined, and the neurologic status remains normal. She is able to typewrite by means of the touch system (not looking at the keyboard) with both hands, both to dictation and to sight. She is not familiar with German; yet she can type passages in German satisfactorily by means of the touch system, using both hands simultaneously. In October 1940 she returned to her former part time position as a social secretary, typing speeches and correspondence. Apparently, she is able to do this work as efficiently as before the partial section of the corpus callosum.

Case 5.—A. M., a white single man aged 25, a former gardener and mill hand, was admitted to the Strong Memorial Hospital on May 7, 1939. He had had grand mal seizures after an injury to the head ten years before. One year before, the fingers of the right hand were amputated after an accident. He was affable, naive and of normal intelligence. The pupils were irregular and reacted poorly to light. Examinations of the blood and spinal fluid, including serologic studies, gave normal results. He was definitely right eyed and right footed in laterality tests, and he had used his right hand predominantly before the accident. He said that after the amputation he learned quickly to use his left hand in writing and other activities.

Operation.—On May 13, 1939 a right frontoparietal craniotomy was performed. The longitudinal sinus was divided at the juncture of the anterior fourth and the second fourth to gain exposure. It was necessary to ligate two veins entering

the longitudinal sinus from the right frontoparietal lobe. The exposure was a most difficult one. The corpus callosum was sectioned from the anterior commissure to a point about 1 cm. anterior to the tip of the splenium. The left fornix was divided at the foramen of Monro (fig. 1).

Course.—For two weeks the postoperative course was stormy, with pyrexia (temperature up to 104 degrees F.) of undetermined cause. During this time the patient was frequently delirious and was too sick to cooperate for detailed neurologic studies. Subsequently he showed no evidence of dyspraxia in the left hand and was as efficient in the use of his right hand as he had been before operation. Since his discharge, on June 20, he has been forced to loaf around, except on the infrequent occasions when he can find a temporary job at bottle washing or gardening. Neurologic studies on several occasions have revealed the same conditions as before operation.

Case 6.—F. P., an Italian boy aged 17, was admitted to the Rochester Municipal Hospital on March 19, 1940. Up to the age of 7 years he was active and of normal weight. He then began to put on weight and had petit mal attacks, consisting of a queer feeling in his abdomen with subsequent loss of consciousness for a minute or less. Grand mal seizures and changes in behavior began at the age of 12 years. He was obese and hypochondriacal, with borderline intelligence and a Binet level of 11 years 2 months.

Physical examination revealed obesity involving chiefly the trunk and thighs, suggestive of pituitary dyscrasia. Except for a small penis and prostate, the external genitalia were normal. The neurologic status was normal. Metabolism and the chemical constituents of the blood were normal. Stereograms revealed that the sella was very small, measuring 7 mm. in its anteroposterior diameter and 5 mm. in depth. Laterality studies were suggestive of some degree of ambilaterality. There was no family history of left handedness. The patient was left handed as a child but was trained to use the right hand by his teachers. At the time of examination he was able to use his right and left hand equally well in drawing or writing. He was definitely right footed and right eyed.

Operation.—On March 22, 1940 a left frontoparietal craniotomy was performed and the entire corpus callosum, except for the tip of the splenium, was sectioned. One large and two small veins entering the longitudinal sinus from the left frontal lobe were ligated.

Course.—The patient was examined as soon as he regained consciousness, on the evening of March 22. He was able to move both hands on request and showed no evidence of dyspraxia in either. The following day the neurologic examination revealed nothing abnormal except for slight weakness of the right arm and leg and slightly increased patellar and ankle reflexes on the right. Detailed tests for praxis gave no evidence of dyspraxia in either hand. He was able to write and draw with either hand as well as before operation. His convalescence was rapid, and on April 23 he was just as proficient in playing the piano and in his tap dancing as before operation. He has been followed in the clinic since his discharge, on May 2, 1940, and has never shown any evidence of dyspraxia.

Case 7.—W. M., a white single girl aged 18, was admitted to the Strong Memorial Hospital on Nov. 2, 1940. Her early development was normal, and she was able to walk and talk at 1 year of age. At the age of 13 months she fell and sustained a fracture of the right parietal portion of the skull. At this time a left-sided paralysis developed, with no aphasia. The paralysis cleared up com-

pletely in six weeks. At the age of 2 years she began to have grand mal seizures. During the past five years the seizures had become more frequent and severe, with numerous petit mal attacks. The grand mal attacks were preceded by an aura of numbness and weakness of the left side. After arousal from the coma the left arm was weak for about one hour. The patient was pleasant, cooperative, but dull, with a Binet age of 9 years 10 months. (A psychometric examination at the age of 11 years 6 months revealed a Binet level of 8 years 8 months.) The physical status was normal. The results of neurologic examination were variable but usually normal. At times when she complained of transient numbness on the left side, slightly exaggerated deep reflexes and hypesthesia from the angle of the jaw down were noted on the same side. This feeling of numbness, according to the patient, was identical with the aura preceding a grand mal seizure. Ventriculographic studies showed no abnormality. Electroencephalographic studies revealed delta waves of large amplitude (50 to 150 microvolts) and a frequency of 3 per second over the entire scalp, although waves of the largest amplitude were found over the right frontal area. Laterality studies revealed right handedness and right footedness and predominant left eyedness.

Operation.—On Nov. 13, 1940 a right frontoparietal craniotomy was performed and the corpus callosum completely sectioned except for a few possible fibers in the splenium. The left fornix was divided. One medium-sized and two small veins entering the longitudinal sinus from the right frontal lobe were ligated (fig. 1).

Course.—Convalescence was rapid. On awakening from the anesthesia the patient could move all extremities, but the grip in the left hand was weak. The following day the grip in this hand was stronger, and the deep tendon reflexes were equal on the two sides. She had complete astereognosis in the left hand. On November 15 (two days after operation) strength as measured by the dynamometer was 18 Kg. in the right hand and 13 Kg. in the left hand. (Before operation strength was 20 Kg. in the right hand and 16.5 Kg. in the left hand.) The deep tendon reflexes were slightly exaggerated on the left side, but ankle clonus and the Babinski sign were not present. Seven days after operation the weakness on the left side was gone. Stereognosis and tactile lexia were intact in both hands. A complete study of praxis as described by Wilson showed no evidence of dyspraxia in either hand. She was able to write with either hand, although she had to be persuaded to write with her left. Incidentally she held the pencil feebly but correctly in her left hand.

Her subsequent course in the hospital was uneventful except for an occasional petit mal attack, which made her discouraged and somewhat depressed. The reflexes became equal on the two sides within a week after operation.

(*b*) *Partial section at the first operation and complete section of the corpus callosum subsequently* (1 case).

Case 8.—E. J. B., a deteriorated, unmarried white woman aged 23, was admitted to the Rochester Municipal Hospital on March 11, 1939. Grand mal seizures began at the age of 9 years, and psychomotor attacks and marked personality changes had occurred during the past six years. She was irritable, untidy and stupid, with a Binet level of 11 years. The physical and neurologic status was not remarkable. Laterality studies revealed right ocular dominance, right handedness and right footedness.

First Operation.—On March 18, 1939 a right frontoparietal craniotomy was performed and the body and the posterior half of the genu of the corpus callosum

were sectioned. The longitudinal sinus was divided at the junction of the anterior and the second fourth (fig. 1).

Course.—Her convalescence was rapid and uncomplicated. She showed no dyspraxia in either hand, and the results of neurologic examination were normal. She continued to have petit mal and grand mal seizures.

Second Operation.—On April 24, 1939 the wound was reopened and the remainder of the corpus callosum sectioned (fig. 1).

Course.—The patient was rather sick for the first two days but subsequently convalesced rapidly. The neurologic status remained unchanged; no dyspraxia in either hand was found, and she could write with either hand with the eyes open or closed. She was discharged May 16, 1939 and has been examined at frequent intervals. No evidence of dyspraxia has ever been observed.

(*c*) *Complete section of the corpus callosum* (2 cases).

CASE 9.—F. O'B., a white married man aged 27, was admitted to the Strong Memorial Hospital on Oct. 11, 1939. At the age of 12 he fell from a railroad car, striking his head on the tracks, and was rendered unconscious. One year later grand mal seizures appeared and had continued. According to his wife, he had shown peculiarities of behavior during the past year. He was a surly, tough-appearing person. Alcoholic sprees were periodic. The physical status was not remarkable. Neurologic examination revealed agnosia for colors (partial), objects and letters in the left homonymous visual field. Perimetric studies of the visual fields, using a 3 mm. white object, revealed normally full fields. An encephalogram taken October 18 showed an enlarged right lateral ventricle and a slight shift to the left of the anterior portions of the lateral ventricles. Laterality studies revealed mixed dominance. He had always written with his left hand but did many tasks with his right. His siblings and parents were right handed, as was his wife and her family, but 3 of the 4 children of the patient and his wife were left handed. He was definitely left eyed and right footed.

Operation.—On Nov. 3, 1939 a right frontoparietal craniotomy was performed and the corpus callosum was sectioned completely (fig. 1).

Course.—After regaining consciousness he showed no evidence of dyspraxia in either hand. During the first week he was mildly confused, especially at night. He would remark: "Damned if I can quite figure things out at times." At these times he was uncertain regarding the names of the staff who saw him daily. Subsequently, he spontaneously commented on almost complete amnesia for events during the first ten postoperative days. He recalled, however, that his hands behaved strangely at this time; he had the sensation that some one was holding his left hand when he actually was grasping his hands. At other times when he was grasping his own hands it felt as though an object was between them. Several examinations during this period showed that stereognosis was intact in both hands. On November 14 the neurologic status was the same as before operation. There was no evidence of dyspraxia, and he could roll a cigaret with his eyes closed. He was able to write with either hand with the eyes open or closed. Since discharge to his home, on Nov. 22, 1939, he and his wife have described the occasional occurrence of peculiar behavior which can best be called diagnostic dyspraxia. This will be described in a future report.[18] Subsequent examinations have revealed no

18. Akelaitis, A. J.: Studies on the Corpus Callosum: IV. Diagnostic Dyspraxia in Epileptics Following Partial and Complete Section of the Corpus Callosum, to be published.

changes in the neurologic status. He has been seen on numerous occasions up to November 1940 because of an infected bone flap, which was removed. He has never shrown signs of meningitis.

CASE 10.—E. K., a white single woman aged 30, was admitted to the Rochester Municipal Hospital on Nov. 6, 1939. Fifteen years ago she sustained an injury to the head, without loss of consciousness. Two years later, at the age of 17, she began to have grand mal seizures. These usually occurred just as she was falling to sleep. She would be awakened by a feeling of numbness in her left arm and would cry out and then lose consciousness. The convulsion would begin with tonic and clonic movements in the left side and subsequently involve the entire body. She was a garrulous, misanthropic, rather stubborn woman.

Physical examination disclosed a rough systolic murmur over the precordium, suggestive of mitral insufficiency. Neurologic examination revealed slight atrophy of the left hand, with normal reflexes and sensory status. The left arm was not as skilful in performance of ordinary tasks as one would expect. The visual fields, taken with a small white object in the perimeter, were full. However, the patient was unable to recognize colors, objects and letters in the left homonymous field, even though she showed no disturbance in absolute or relative localization in this field. A ventriculogram showed marked dilatation of the temporal and occipital horns, as well as of the posterior end of the body of the ventricle, as evidence of a scar in the right temporo-occipital region. Laterality studies revealed left eyedness. right handedness and right footedness.

Operation.—On Nov. 20, 1939 a right frontoparietal craniotomy was performed and the corpus callosum was completely sectioned. Two veins of considerable size had to be ligated to allow retraction of the right frontal lobe from the midline (fig. 1).

Course.—The patient's behavior for the first two weeks was peculiar in that she was usually mute, would assume cataleptoid postures and appeared confused. She could move her extremities normally on request, and the reflexes were equal on the two sides. On November 30 she executed correctly various movements on request, such as touching her right ear with her left hand, and wrote answers to questions but remained mute. To the question: "How do you feel?" she wrote with her right hand: "I feel much better than I have in over two weeks." With her left hand she wrote "cat" on request, but "dog" was written illegibly. Subsequently examinations for tactile lexia and stereognosis could be carried out if the patient was allowed to write her answers. She showed no disturbance of these functions. The muteness gradually cleared up, and she became normally responsive on December 9. On this date she was found sitting in a chair embroidering. She was able to sew with her left hand in a clumsy manner and remarked: "I have never been any good with my left hand in sewing or anything else." She wrote with either hand with the eyes open or blindfolded. With the eyes open she was able to write with either hand and deal cards simultaneously with her other hand. The neurologic status remained the same as before operation.

Subsequent Course.—Since discharge from the hospital, on Dec. 22, 1939, she has been seen in the clinic on several occasions, and no evidence of dyspraxia has been observed by the examiners or her family. She continues to have infrequent attacks, which occur just as she is falling off to sleep. However, the attacks are now limited to numbness and clonic movements in her left side, with no loss of consciousness.

GROUP 2: CASES IN WHICH THE MOTOR ASPECTS OF THE NEUROLOGIC STATUS WERE NORMAL BEFORE OPERATION BUT EVIDENCE OF CEREBRAL DAMAGE WAS PRESENT POSTOPERATIVELY

(3 CASES)

(*a*) *Partial section of the corpus callosum* (2 cases).

CASE 11.—W. S., a white, single farm hand aged 27, was admitted to the Strong Memorial Hospital on Feb. 14 and May 3, 1939. Since an injury to the head ten years before, he had had grand mal seizures. He was an emotionally undemonstrative, rabelaisian fellow, with an expressionless face. The physical and neurologic status was not remarkable. Laterality studies revealed right ocular dominance, right handedness and right footedness.

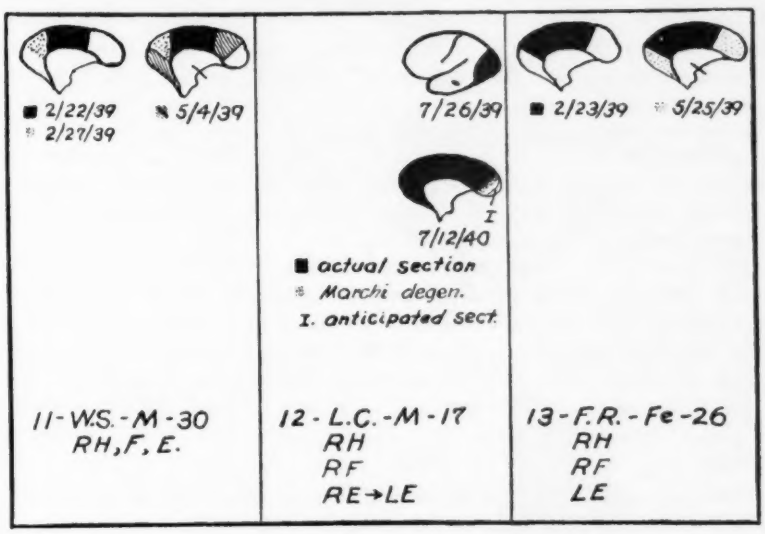

Fig. 2 (group 2; cases 11-13).—Diagrams to illustrate the degree of surgical section of the corpus callosum, as described in the operative notes.

First Operation.—On Feb. 22, 1939 a right midparietal craniotomy was performed and the body of the corpus callosum sectioned. This patient was the first one having an intact brain in whom a section of the corpus callosum was attempted. It is now recognized that the exposure was made farther forward than was necessary. Three veins draining the arm area were ligated in order to gain exposure of the corpus callosum (fig. 2).

Course.—The patient appeared drowsy, and the left arm and leg were weak. He had many seizures, some limited to the left side and others generalized. Reelevation of the bone flap to determine the source of postoperative bleeding was decided on.

Second Operation.—On February 27 the wound was reopened, and the ligated veins going from the right frontal lobe to the longitudinal sinus were observed to be thrombosed well into the arm area. A large vein extending well down

toward the arm area showed retrograde thrombosis. The posterior half of the genu of the corpus callosum was also sectioned at this time (fig. 2).

Course.—The weakness of the left arm and leg persisted, and the patient complained of dysesthesias in the left hand. The deep reflexes on the left side were increased, but the response to plantar stimulation was normal. He had slight weakness of the lower left side of the face. Adiadokokinesis and marked disturbance of finer movements were present in the left hand.

On March 21, 1939 the neurologic status was found to be the same. Spontaneity was decreased. He walked slowly and with slight generalized flexion, with few associative movements of the arms. Speech was monotonous and slightly dysarthric. He showed no disturbance in handling objects presented to him and imitated movements performed in front of him. He was able to perform, clumsily with his left hand, simple movements, such as snapping his fingers, making a fist and thumbing his nose. Expressive movements, such as threatening, beckoning, waving good-by and saluting, could be carried out. Movements directed toward a definite object, the material not being at hand, such as catching flies, playing the piano or putting a stamp on a letter; purposive movements with objects in his hand, such as lighting a candle, smoking, brushing his sleeve or using a lock, and reflexive movements, such as touching various parts of his body, could all be carried out with his left hand in an awkward manner. He could perform these acts with the eyes open or closed. The right hand was entirely normal. He showed no difficulty in eating or dressing except for a certain slowness. He was discharged home on March 26, 1939.

The grand mal seizures returned, and he was readmitted to the hospital on May 3, 1939. The neurologic status remained unchanged. He was concerned over the weakness of the left hand and remarked that he was unable to play his steel guitar because he did not have the power to press his fingers down on the strings. He was considered the best card player among the patients in the division.

Third Operation.—On May 4 the old wound was reopened, and the remainder of the corpus callosum except for the posterior centimeter of the splenium was sectioned. The right fornix was divided (fig. 2).

Course.—Convalescence was uneventful. On the day of discharge, May 25, he showed no dyspraxia in the left hand except for slight clumsiness. He was able to write with either hand with the eyes open or closed.

On Dec. 6, 1939 neurologic examination revealed slight weakness of the left hand and leg, with increased deep reflexes on the left side and moderate ataxia of finer movements in the left upper extremity. Except for the ataxia, praxis was not disturbed in the left hand. He could roll a cigaret with either hand with the eyes open or closed. He was able to write with either hand and at the same time deal cards with the other.

The receptive and expressive aspects of music were tested under the guidance of a professional guitarist, Mr. Joseph Petite. The patient appreciated correctly the position of the guitarist's fingers on the stringboard required to produce various chords but was unable to name the chords struck when blindfolded. He was able to place the fingers of his left hand correctly on the stringboard for various chords requested by the examiner and strike the strings with his right hand. This he could do more quickly when blindfolded than when looking at the board. In spite of this, he was unable to play a melody because he could not change the position of his left hand quickly enough. He was unable to tap, with either hand, in rhythm

to various popular selections played by a marimba and guitar duet. He could not carry a melody when singing in a group. It was concluded that the patient had lost all sense of musical rhythm.

CASE 12.—L. C., an Italian youth aged 17, was admitted to the Strong Memorial Hospital on July 1, 1940. In 1936 the patient was struck by an automobile and sustained a compound fracture of the left side of the skull, which necessitated

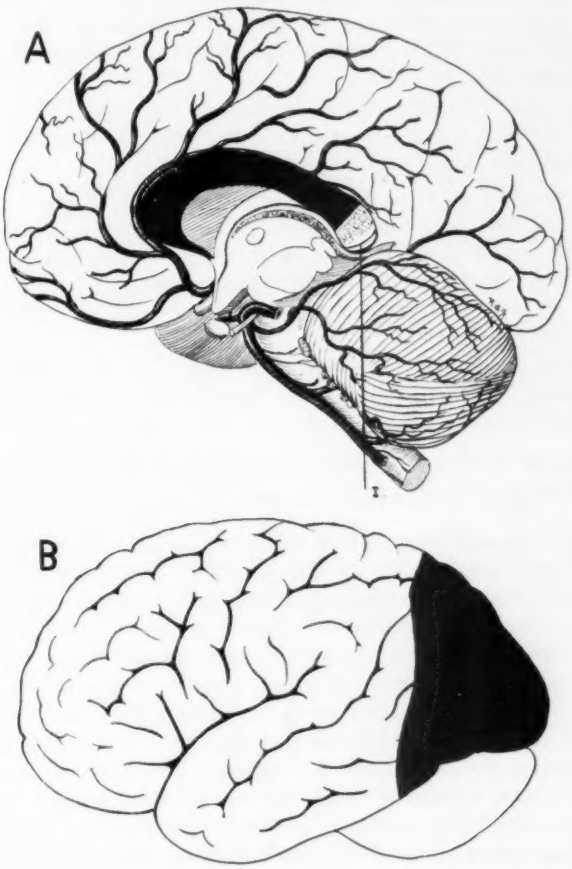

Fig. 3 (case 12).—*A*, diagram illustrating the anticipated section of the corpus callosum, as described in the operative note (*1*); the actual section, as shown at autopsy (shaded in black), and the extent of degenerated fibers, as obtained with Marchi studies (stippled portion). *B*, extent of resection of the posterior portion of the left cerebral hemisphere, as observed at autopsy.

a plastic repair of the skull and an operation on the scalp. Four months later he began to have grand mal seizures, starting with flashes of light in the right homonymous field, and right-sided jacksonian attacks. He was a cheerful, rather jocular lad.

The physical status was normal except for a moderate degree of obesity. The neurologic examination revealed nothing abnormal except for complete right homonymous hemianopia. Laterality studies revealed right ocular dominance, right footedness and right handedness. A scar in the left temporo-occipital region revealed in clinical and ventriculographic studies was considered the pertinent lesion

On July 26, 1939 the left occipital lobe was resected. Right hemiparesis developed, and on July 30, 1939 a subdural space clot was evacuated. The hemiparesis cleared, and he was discharged home on Aug. 31, 1939. The convulsions returned in their original form, and he was readmitted July 1, 1940. The physical and neurologic status remained the same as on the previous admission. However, ocular dominance had changed to the left eye.

Operation.—On July 12, 1940 a right frontoparietal craniotomy was performed and the entire corpus callosum except for a few fibers in the tip of the splenium was sectioned (figs. 2 and 3).

Course.—On July 15 he showed no difficulty in using his hands and sensation was intact. On that day and on the following day he had two right-sided seizures, and it was observed that although the power in his left arm was good, he showed difficulty in carrying out commands requiring finer movements with his left hand. On July 22 he had two severe seizures involving the right side and died shortly after the second convulsion.

Autopsy.—A large subdural hematoma lay over the right frontal lobe. The point of bleeding could not be made out but was thought to occur from a tributary of the longitudinal sinus (fig. 2).

(*b*) *Partial section of corpus callosum at the first operation and complete section of corpus callosum subsequently* (1 case).

Case 13.—F. R., a white unmarried woman aged 26, was admitted to the Strong Memorial Hospital on Feb. 19 and May 23, 1939. She sustained Erb's palsy on the left side at birth and was successfully treated for congenital syphilis. She had been subject to grand mal seizures since the age of 2 years. She was a shy, sensitive, kindly woman, with a Binet level of 18 years 2 months. She had the unusual ability to play a new melody on the piano without notes after hearing it once. The physical examination revealed widely separated, peglike teeth; atrophy of the left arm and shoulder, with contraction of the biceps muscle, limiting extension to 145 degrees at the elbow, and an infantile uterus. Neurologic examination disclosed horizontal nystagmus in all lateral deviations, vertical nystagmus in upward gaze and absence of the biceps reflex on the left. Laboratory studies, including Wassermann tests of the blood and spinal fluid, gave negative results. Laterality studies showed left ocular dominance, right handedness and right footedness.

First Operation.—On February 23 a right midparietal craniotomy was performed and the body and the posterior half of the genu of the corpus callosum were sectioned. Two small veins entering the longitudinal sinus from the right parietal lobe were ligated in order to allow separation of the cerebrum from the falx (fig. 2).

Postoperative Course.—The first two days of the postoperative course were characterized by marked psychomotor retardation, dysarthria and paraphasia, weakness of the left arm and inability to perform movements with the left hand on

request. Sensory examination revealed hypesthesia and astereognosis in the left hand. She convalesced slowly, complaining of dysesthesias in the left arm and leg and weakness of the left hand. The ankle and patellar reflexes were increased, and ankle clonus could be elicited on the left side. On March 21 she expressed paranoid ideas, stating that the neurologic examinations were performed to prove to the other patients that she was insane. She became suspicious and depressed, and it was considered inadvisable to retest her. Speech was slow and dysarthric. Her Binet level had fallen to 16 years 9 months. She was discharged home on March 26.

At home the patient continued to be depressed and retarded. For three weeks she was troubled by a peculiar antagonism or incoordination between the two sides of the body, which may best be described as diagnostic dyspraxia. The patient noted that frequently her left hand would do exactly the opposite of what her right hand was doing. For example, she would open a door or drawer with her right hand and push it shut with her left hand, or put her dress on with her right hand and pull it off with her left hand. This diagnostic dyspraxia showed itself in more general activities, such as desiring to walk forward or stand up from a sitting position and being unable to do so because there seemed to be an equal urge to walk backward or remain seated. She was unable to play the piano because of the weakness and clumsiness in her left hand.

Grand mal seizures continued, and she was readmitted on May 23. The neurologic examination disclosed dysarthria, exaggerated deep reflexes on the left side (except for absence of the biceps reflex), weakness of the left arm and leg and hypesthesia to light touch and hyperesthesia to pinprick over the left side.

Second Operation.—On May 25 the old wound was reopened and the bone flap reflected. The remainder of the corpus callosum and the left fornix were sectioned (fig. 2).

Postoperative Course.—The depression continued, but the course was otherwise uneventful. Neurologic examination on June 10 revealed exaggerated deep reflexes in the left lower extremity, an equivocal Babinski response on the left side but no evidence of dyspraxia in the left hand. Sensory examination showed nothing remarkable except for diminution of vibration sense in the left leg. Stereognosis was intact. She was able to write with either hand with the eyes closed. She was discharged home on June 11.

Subsequent Course.—For the following four months she continued to be retarded and depressed and exhibited many abnormal traits, such as fear of contamination, irritability, fatigability, seclusiveness and impaired memory for recent events. She tried to crochet, without success, and had difficulty in playing the piano. For example, she would play correctly a few opening bars of familiar compositions, such as Dvorak's "Humoresque" or Drdla's "Souvenir," and then stop, being unable to continue. Since she played mostly by ear, this difficulty was due to a memory defect rather than to any actual dyspraxia.

On September 28 she was readmitted for a complete check-up. The neurologic status was the same as on June 10. No evidence of tactile alexia or dyspraxia was found in either hand. She was able to write spontaneously and to dictation with either hand with the eyes open or closed. She expressed discouragement over the fact that she was still having seizures in spite of surgical and medical therapy and felt that her future was hopeless. Several psychotherapeutic sessions resulted in diminution of the depression.

She was studied in detail in August 1940. She was no longer depressed, and there was no evidence of the "catastrophe" reactions [19] which she showed so readily in the examinations following operation. The neurologic status revealed absence of the left biceps reflex and slightly hyperactive deep reflexes in the left lower extremities, with a normal plantar response. Elaborate studies of praxis showed no greater disturbance in the left hand than was evident before operation. She played very well with both hands and without the use of notes such melodies as Romberg's "Auf Wiedersehen," Nevin's "Mighty Like a Rose" and Strauss's "Blue Danube Waltz." From notes she played the "Wedding March" from Wagner's "Lohengrin" with only moderate success. By the touch system entirely, and using both hands, she typed fairly well, making a number of mistakes, but these were within the correct limits of each hand position on the keyboard. These mistakes were made as often with the right hand as with the left. She typed sentences in English as well as in German. She had no reading or speaking knowledge of German.

GROUP 3: CASES IN WHICH EVIDENCE OF CEREBRAL DAMAGE (DIFFUSE OR FOCAL) WAS PRESENT BEFORE OPERATION (5 CASES)

(*a*) *Partial section of the corpus callosum* (2 cases).

CASE 14.—M. L. P., a white girl aged 10, was admitted to the Strong Memorial Hospital on March 12, 1940. Up to the age of 3 years she developed normally, having learned to walk and talk satisfactorily. At the age of 3 she was struck over the left parietal region by a falling object and two weeks later had her first grand mal seizure, which was followed by status epilepticus, of five hours' duration. After she aroused from the coma, aphasia and right hemiplegia, with external strabismus, were observed. The strabismus improved after three weeks, and she learned to talk after two months. The paralysis improved gradually, so that at the time of admission her gait was only slightly spastic and she showed only slight clumsiness in her right hand. She had remained free of seizures until six months ago, when she began to have frequent petit mal attacks. During this time she had shown increasing irritability and easy fatigability. According to her teacher, the child was alert and industrious in the morning but became drowsy and indifferent in the afternoon. She was an attractive, coy, cheerful, cooperative girl, with a Binet level of 9 years 9 months. She had always bitten her nails.

The physical status was not remarkable. Examination of the cranial nerves revealed external strabismus on the left side, defective vision (3/60) in the left eye and agnosia for colors, objects and letters in the right homonymous field with normally full visual fields to movement as determined by perimetric tests. She showed residua of right hemiplegia, with increased motor tonus, exaggerated deep reflexes and a positive Babinski sign on the right. Sensation, including two point discrimination, stereognosis and tactile lexia, was intact in each hand. Except for a slight amount of awkwardness in the right hand, she was able to perform various praxic functions surprisingly well but could not shuffle playing cards. She could write with either hand with the eyes open or closed.

An encephalogram revealed an old atrophic lesion of the left cerebral hemisphere, with associated hydrocephalus involving the ventricle on this side and

19. A term employed by Kurt Goldstein (The Organism, New York, American Book Company, 1939) to denote the disordered responses in subjects undergoing study.

shifting of all the ventricular structures toward the left. Laterality studies revealed right ocular dominance, left handedness and left footedness. Undoubtedly the left cerebral hemisphere had been dominant until the age of 3 years. All members of the family were right handed.

Operation.—On March 29, 1940 a right frontoparietal craniotomy was performed and the corpus callosum sectioned almost completely except for the posterior 0.5 cm. The left fornix was divided (fig. 4).

Course.—On awakening from the anesthesia the patient was able to move both sides, and grasp reflexes were observed bilaterally. The following day the grasp reflex was present in the right hand only, and motor strength was good in each hand. The forced innervation in the right hand was present irregularly for one month after operation. On April 3 she had a seizure on the left side. On April 4

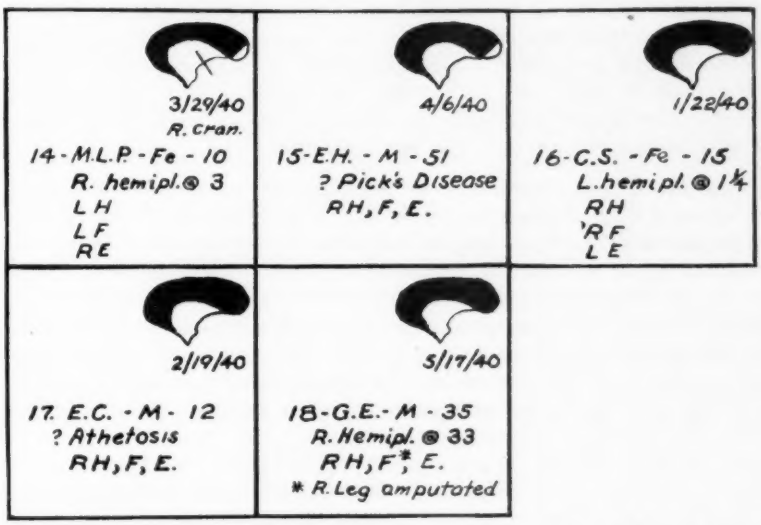

Fig. 4 (group 3; cases 14-18).—Diagrams to illustrate the degree of surgical section of the corpus callosum, as described in the operative notes.

she was able to write with either hand with the eyes open. She tended to perseverate when writing with the left hand. Perseveration in tasks and conversation was prominent for the first four weeks of her postoperative course. On April 6 a cough developed, and Haemophilus pertussis was isolated.

Because of her perseveration and poor grasp of the examiner's requests, detailed studies could not be made until a month after operation. During this interval, however, she was able to manipulate her wheel chair satisfactorily and handled food with a fork in her right hand as well as before operation, but she could not be induced to cut meat with the knife in her right hand.

On April 23 the neurologic status was essentially the same as before operation except for astereognosis in the right hand. However, two point discrimination and interpretation of skin writing were not disturbed on the right side. Usually praxic functions were no more disturbed in the right hand than before operation, but occasionally she showed an increased degree of ataxia. She could write with

either hand with the eyes open or closed as well as she did before operation. The evident decline in her mental ability was corroborated by psychometric studies, which disclosed a Binet level of 7 years 6 months. She was discharged home on May 18, 1940.

Subsequent Course.—The menarche was established shortly after her discharge from the hospital. The family noted some slowing in her mental ability, due in most part to memory defects. She did not "act as bright" as she had before operation. The irritability with various members of the family became more noticeable. She started back to school in September 1940, in the fifth grade (the same as in the preceding year), and the teacher noted that the child's fatigability was more marked than before. She would attack a new problem with enthusiasm but would quickly become indifferent. Since discharge she had had three petit mal attacks, associated with adversive movements of the head and eyes to the left, and one grand mal seizure.

She was readmitted to the hospital on Nov. 7, 1940 for a complete check-up. The neurologic status was essentially the same as on April 23. Her performances in various praxic tests with the right hand remained the same as before operation. She was able to write with either hand. Psychometric study gave her a Binet level of 8 years 8 months, a decided improvement over the results of the first postoperative studies, but still far below her preoperative level.

Case 15.—E. H., a white married man aged 51, employed as a stock clerk, was admitted to the Strong Memorial Hospital on March 26, 1940. In 1936 the patient had three grand mal seizures, beginning with a cry, adversive movements of the head to the left and tonic movements of the left arm, followed by a generalized seizure. He was free of seizures for nine months and in the fall of 1937 had another series of three convulsions. In the fall of 1938 several seizures occurred within a short period. In the fall of 1939 he had two attacks a month for three months. One week before admission very frequent seizures developed, and on the day of admission he was having a seizure every ten minutes. He had always been a tense, worrisome, conscientious man.

On admission he was having a seizure every fifteen minutes. It would be initiated by a loud howl, followed by generalized muscular tenseness, twitching of the facial muscles and occasional spasmodic clutching movements of both hands. The head was turned to the left, and the eyes were in left conjugate deviation. Between these attacks he was cooperative but paraphasic, with some dysgraphia in the right hand. Physical examination revealed nothing remarkable. Neurologic examination disclosed transient mild weakness of the right lower part of the face, nystagmus on right lateral gaze and swaying in the Romberg position.

Preoperative Course.—Twenty-four hours after admission the seizures ceased, but the patient remained paraphasic until March 30. At this time the neurologic signs had cleared. On April 2 a complete neuropsychiatric study presented evidence of confusion of an organic reaction type, with disturbances in the sensorium, mental capacity and intellect. "Catastrophe" reactions were likely to occur. He showed no dyspraxia or tactile alexia in either hand and could write with each hand with the eyes open or closed. He was unable to draw a cube in spite of numerous leads from the examiner but had no difficulty in copying complicated bidimensional designs. Ventriculograms taken March 30, 1937 and March 28, 1940 were normal. The clinical findings and history suggested Alzheimer's or Pick's disease. Laterality studies disclosed right ocular dominance, right footedness and

predominantly right handedness. As will be seen in the report on the postoperative course, the left hemisphere was dominant for speech.

Operation.—A right frontoparietal craniotomy was performed on April 6, 1940 and the corpus callosum completely sectioned except for a few possible fibers in the tip of the splenium. A large vein entering the longitudinal sinus from the right frontal lobe was ligated. The cortex was atrophic, with small convolutions. The atrophy was more marked toward the frontal pole (fig. 4).

Biopsy.—A small core (1 cm. in diameter) of tissue from area 9 of Brodmann was removed for study. Diffuse loss of nerve cells was observed throughout the third, fifth and sixth layers, with a moderate number of sclerosed nerve cells undergoing phagocytosis by neuroglia cells. There was slight gliosis throughout the cortex and subcortex. The blood vessels were not remarkable. No senile plaques were present in Braunmühl preparations. Numerous round, homogeneous argentophilic bodies were seen in the nerve cells and lying free in the parenchyma. These changes were suggestive of Pick's disease.

Postoperative Course.—For the first two days the patient was in a semicomatose state, the cause of which was not apparent from clinical or laboratory studies. On April 10 he would squeeze hands on request. The left hand grip was very weak, and the left leg was limp and moved infrequently. He would touch his nose with his right hand on request but could not do so with his left hand. However, on one occasion he spontaneously brushed his nose with his left hand. A grasp reflex was irregularly present in the left hand for the next ten days. It was likely to appear when the patient was fatigued or confused. On plantar stimulation the big toe on the left side went into dorsal extension. He was unable to wave good-by with his left hand, and astereognosis was present in this hand.

On April 15 he was apprehensive but was oriented for time, place and person. Reflexes were active and equal on the two sides, but strength in the left hand and the left foot was diminished. Astereognosis prevailed in the left hand, and there was hyperesthesia on the left side. He showed difficulty with voluntary movements of the left arm and became confused and increasingly apprehensive whenever one studied the functions of the left side. On repeated requests, when his right hand was restrained he was unsuccessful in touching his nose with his left hand but finally did so impulsively and awkwardly. Prior to this he had spontaneously scratched his neck with his left hand. He was able to write fairly well with his right hand while holding the pad in his left hand. His writing was slow and preceded by much deliberation, and he misspelled day as "dauiy." When asked to transfer the pencil to his left hand and the pad to his right hand he seemed confused and made no movement. The examiner had to transfer the articles, and after the pencil was placed correctly in his left hand he made efforts to transfer it back to the right hand. He was unable to write. He was asked to transfer the pencil back to the right hand, reached for it and grasped it but held on tightly to it with his left hand. He finally pulled the pencil out of his left hand but made occasional grabs for it with his left hand. On request he then readily transferred the pencil back to his left hand from his right hand.

On April 16 it was observed that he would make no effort to write with the left hand and wrote poorly with the right hand. He was able to read fairly well, and there was no evidence of an expressive or a receptive form of aphasia. When asked to make a fist with his left hand he invariably placed his right index finger in the left palm and closed his fingers over it. However, when the right hand was restrained he would make many futile efforts to close his left hand, with

simultaneous clenching of the right hand. As soon as one placed an inanimate object in his left palm his fingers closed over it adequately, and it was difficult for him to release the object. Strangely enough, if the patient's or the examiner's finger was used as a stimulus he relinquished his hold on request with no difficulty. In all tests in which the right hand was tested the patient showed no confusion, but he became confused whenever one tested the left side for motor or sensory functions. His behavior when striking a match from a paper cover was instructive. When asked to strike a match he took the cover in his left hand, opened it, pulled out a match, struck it against the cover and then blew it out. When asked to strike a match with his left hand he became confused and continued to strike match after match with his right hand. Finally the cover was taken out of the left hand and placed in his right hand, and he was asked to light a match with his left hand. After much deliberation he opened the cover with the left hand, fingered the matches for a long time, finally chose one, then began bending it back and forth and at the same time tried to close the cover. He became increasingly confused, and he was relieved of this task after five minutes of fruitless effort. The examiner then removed a match from the cover and placed it in his left hand. He held it correctly and proceeded to strike the cover, which he held in his right hand, against the match for several minutes, without effective results. This discouraged him after a while, and he put the cover into his left hand and continued to hold both the match and the cover in this hand. Later that day he was observed eating, and he showed no disturbance in buttering his bread or in bringing it to his mouth with his left hand.

On April 24 the deep reflexes were active and equal on the two sides but the weakness of the left side persisted. He showed astereognosis in both hands but had no difficulty in naming objects which he saw before him and recognized a watch by its ticking. He was able to write with either hand with the eyes open. The striking of a match with his left hand gave him a good deal of trouble for five minutes, but finally, in an impulsive manner, he pulled the match off the cover and struck it successfully, exclaiming: "There, I got it," and blew it out.

The following day he had several seizures on the left side. He was able to roll a cigaret, using both hands, lighted it satisfactorily with his left hand and held it in his left hand throughout its smoking.

On April 27 he was confused and, when tested in the examiner's office, showed marked "catastrophe" reactions. Whenever a task was too difficult he would show perseveration and then have urgency of urination or defecation. His confusion became so marked that he could not be tested further.

Beginning on April 30 and continuing for three days he had numerous seizures, most of which were right-sided jacksonian fits. Right hemiplegia with aphasia developed. During this time it was observed that he could use his left hand well in eating. Although unable to speak except for "Ah huh," he showed no difficulty in understanding spoken requests. Unfortunately the left hand was not tested for writing at this time.

On May 4 his speech returned to some degree, and three days later he was able to read the headlines of a paper, but probably with little appreciation of the contents. The hemiplegia cleared, and the patient was discharged home on May 9, 1940 in only fair condition. He showed no dyspraxia or aphasia but was likely to become confused easily.

Subsequent Course.—On May 30, one of us (W. A. R.) visited the patient at his home and was surprised at his improvement. He had had no seizures since his discharge, and his behavior, interests and memory were fairly normal. He

inquired about the various physicians and nurses at the hospital and spontaneously remarked about his lacunar amnesia for periods of his postoperative stay in the hospital. The results of neurologic examination were essentially without significance except for a slight degree of forced innervation in the right hand. No astereognosis or dyspraxia was observed in either hand, and he was able to write with either hand.

He returned to the hospital on Aug. 22, 1940 for a check-up examination before returning to work as a janitor in a telephone corporation. He appeared apprehensive but cooperative and apologetic. He showed disturbances in calculation and defects in recent memory and immediate retention. The neurologic status revealed questionable hypesthesia (tactile and vibration senses) over the right lower extremity. Praxis was intact in each hand. He could write with either hand, with the eyes open or closed, a dictated or spontaneous sentence. In contrast to his difficulty to draw objects in three dimensions before operation, he now could draw cubes, cones, etc., with ease.

(*b*) *Complete section of the corpus callosum* (3 cases).

CASE 16.—C. S., a white girl aged 15 years, was admitted to the Strong Memorial Hospital on Jan. 4, 1940. The patient developed normally in infancy and walked at the age of 12 months. At the age of 15 months she had "encephalitis" associated with convulsions and hemiplegia involving the left side. In three months she learned to walk again but always limped. As a result of much physical therapy, she learned to use her left hand to knit and crochet but was unable to play the piano or to typewrite. At 5 years of age she began to have petit mal attacks, and at 11 years grand mal seizures set in. She was a sociable, cheerful girl, whose Binet level was 12 years 4 months.

Except for slight underdevelopment of the left side of the body, the physical status was good. Neurologic examination revealed mild residual left hemiplegia, with slight weakness of the lower left side of the face, slightly increased tendon reflexes and muscle tonus on the left side and a suggestive Babinski response to plantar stimulation on the same side. No forced motor innervation was observed in the left hand. The gait was a bit unsteady, with a tendency to walk to the left, and the left arm was slightly adducted and flexed, with loss of associated movements. She was able to write with either hand when the eyes were open. She showed difficulty in doing so with the left hand when blindfolded. Sensation, including stereognosis and tactile lexia, was intact on both sides. Two point discrimination was equal on the two sides. Laterality studies showed left ocular dominance, right handedness and right footedness.

Operation.—On January 22 a right frontoparietal craniotomy was performed and the corpus callosum was completely sectioned. The exposed cortex showed a moderate amount of atrophy. No veins were ligated (fig. 4).

Course.—After regaining consciousness the patient moved her right side well, the left leg fairly well and the left arm very little.

The next day, January 23, she was oriented but did not realize she had been operated on. She was able to move her left leg well, but it was noted that in turning herself from a prone position over to the right side she did not use her left arm. The following day she was confused, and the left arm was moved very little. On January 26 she showed a fair hand grip on the left side but stated that she had no feeling in the left arm or leg. In tests of the left hand for stereognosis (which was intact in the right hand) she made no motor or vocal response when an object was placed in the palm.

On January 27 she showed a strong grasp reflex in the left hand. She could light and extinguish a match with her right hand with no difficulty. In performing this task with her left hand, with her eyes open, she showed great difficulty in removing a match from the matchbox and eventually spilled the box over the bed. A match was then placed in her left hand, which she held awkwardly, and she proceeded to strike the box held in her right hand against the match, finally lighted it and extinguished the flame by blowing. She was requested to pantomime the act of placing a stamp on an envelope with her left hand. She put her tongue out, moved her left hand toward but did not reach her mouth and then pressed her left thumb down on the bed. In this process she would often look at her right hand, which was also performing the pantomime act. She was able to perform movements of expression with her left hand; she beckoned, waved good-by and made a fist weakly to express a threat.

On January 29 a neurologic examination revealed increased reflexes, with a Babinski response and hypesthesia on the left side. Finer movements and diadokokinesis were much disturbed in the left hand. She showed complete astereognosis and inability to recognize figure writing or wooden letters on the left side. She was able to name, point out and move fingers of the left hand and other parts of her body touched while she was blindfolded. A detailed test for praxis, with special attention to the left side, showed little spontaneity, and her mimicry and gestures were very limited. Movements conditioned by visual stimuli on the left side were awkward; she used her left hand while buttering her bread and imitated movements awkwardly with her left hand but showed no difficulty with her right hand. Similarly, she showed disturbance in the left hand because of awkwardness in simple movements, such as making a fist or snapping the fingers; in movements of expression, such as beckoning or waving good-by, and in movements for definite objects, the material not being at hand, such as catching a fly, knocking at a door, playing a piano or threading a needle. In the pantomime act of lighting a candle with her left hand she showed confusion. She would "strike" the match, "apply" it to the candle and bring her hand down on the bed. When reminded that the match was still afire, she seemed perplexed and finally blew out the candle. This response was repeated several times in the same manner. She had no difficulty with this pantomime act when using her right hand. In the performance of purposive movements with objects in her left hand, such as taking money out of a wallet or lighting a candle with a match, and reflexive movements, such as brushing the hair or teeth, she did fairly well except for a certain degree of ataxia. She was unable to write with her left hand, holding the pencil awkwardly between the forefinger and the middle finger, but wrote well with her right hand. However, she was able to write "cat" and "it" in the air by making movements from the left shoulder.

On February 5 forced motor innervation, variable in degree, was noted in the left hand, but pulling on the flexor muscles did not result in closing of the hand. She would squeeze the examiner's hands with both hands on request, and when asked to relax her grip she did so immediately with her right hand but would squeeze tighter with her left. Stroking the dorsal aspect of the left hand did not result in contraction of the extensor muscles. (Schuster and Pinéas.[20]) If her attention was distracted the flexors of the left hand relaxed quickly.

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20. Schuster, P., and Pinéas, H.: Weitere Beobachtungen über Zwangsgreifen und Nachgreifen und deren Beziehungen zu ähnlicher Bewegungstörungen, Deutsche Ztschr. f. Nervenh. **91**:16, 1926.

On February 19 she was seen handling her fork with her left hand satisfactorily. Forced innervation prevailed in the left hand when she was requested to let go of the examiner's hand. Later that day she was seen operating her wheel chair, and in the process of getting through narrow passages she showed no difficulty in controlling the direction of the wheels. There was no evidence of clumsiness or forced innervation in the left hand as she manipulated the chair.

Until her discharge, on March 4, the patient's condition remained essentially unchanged. The forced motor innervation in the left hand had diminished greatly but was present in mild degree occasionally. She had regained her spontaneity, and gait remained essentially the same as before operation. Occasional athetoid-like movements were observed in the left hand. The cranial nerves were intact except for slight weakness of the lower left side of the face. The tendon reflexes on the left side were increased, and a Babinski response was elicited on the same side. The strength in the left extremities was diminished. Sensory examination revealed disturbances of all modalities over the left side. Two point discrimination was as follows:

	Right Hand	Left Hand
Tip of middle finger	0.5-1 mm.	10 mm.
Palm	2 mm.	30 mm.
Dorsum	9 mm.	80 mm.

The patient showed asterognosis and tactile alexia in the left hand when using wooden letters. However, skin writing was correctly interpreted over the left side. The dyspraxia in this hand was due predominantly to ataxia, and in various movements it was evident that the essential idea of the movement was intact. Proprioceptive sensation had returned sufficiently to allow her to write with her left hand with the eyes closed.

CASE 17.—E. C., a white boy aged 12, was admitted to the Strong Memorial Hospital on Feb. 15, 1940. At the ages of 2 and 5 years, respectively, he had a fall in which he struck his head but did not lose consciousness. At the age of 7 he began to have petit mal seizures, often followed by uncontrollable laughter for thirty minutes. Three years later grand mal attacks began, usually ushered in by a feeling of numbness on his right side. Since then he had shown mental deterioration associated with behavior changes, such as irritability and combativeness. He was an irritable, frequently uncooperative boy striving for attention, with a Binet level of 10 years 10 months and an intelligence quotient of 86. He had a talent for drawing, which he did exceptionally well.

Except for enlarged tonsils and several carious teeth, the physical status was good. He was preoccupied, and frequently appeared cataleptoid. He would sit with his hands lying on his lap, with the palms turned upward. Occasionally he showed athetoid-like movements in the upper extremities. The deep reflexes in the left lower extremity were occasionally hyperactive, and on several occasions dorsal extension of the large toe was observed on plantar stimulation of the left foot. The cranial nerves were not remarkable except for a refractive error in the left eye; vision in this eye was 6/60 and could be corrected to 6/30 with lenses. A ventriculogram revealed uniform dilatation of the entire ventricular system. Electroencephalograms disclosed slow (3 to 4 per second) delta waves with an amplitude of 5 to 40 microvolts over the entire calvarium. Laterality studies showed right eyedness, right footedness and right handedness. The father was left handed, left footed and, although ocular dominance varied with different tests, predominantly left eyed.

Operation.—On February 19 a right frontoparietal craniotomy was performed and the corpus callosum was completely sectioned. The cortex appeared to be slightly atrophied, judging from the enlarged subarachnoid spaces (fig. 4).

Postoperative Course.—The postoperative course was complicated by the occurrence of numerous seizures best described as terror spells. These were of short duration, varying from thirty to ninety seconds, associated with loss of consciousness and followed by aphasia and confusion for two minutes or longer. Generally after an attack the patient had amnesia for a period as long as ten minutes preceding the attack. The attack would be ushered in by an expression of terror, with facial pallor and widely dilated pupils, followed shortly by a shrill cry. The right leg and arm would become rigid, and after fifteen or thirty seconds the left arm would begin making defensive movements before his face. At times he would rub his face with the left hand vigorously, crying out in a frightened manner repeatedly. These attacks produced fluctuating neurologic and psychobiologic symptoms, and it is consequently impossible to evaluate properly the clinical picture resulting purely from the section of the corpus callosum.

In the evening following operation he responded and moved both arms on request. The next day the right hand grip was weaker than the left. The tendon reflexes were active and equal on the two sides. On February 23 strength in the two hands was equal and the reflexes were in order. The following day he was able to write his name with either hand with the eyes open, but when asked to write "cat" he continued to write his name. He was confused, and this became accentuated when he was asked to use his left hand. Astereognosis was evident in the left hand. His condition remained static until March 3 and 4, when he had grand mal and jacksonian seizures on the right side, which left him with weakness of that side. On March 9 he showed astereognosis in both hands; this may have been due to his confusion. He was unable to use the right hand and fed himself satisfactorily with his left. He could write with his left hand. He continued to have numerous "terror" attacks. On March 11, although the right arm was very weak, he showed no astereognosis in the right hand, but was unable to identify objects in his left hand. He was allowed to be up in a wheel chair on March 18, and although the weakness in his right arm was evident to some degree and he was awkward in touching his nose with his right hand, he propelled the wheel chair with his hands efficiently. Astereognosis still persisted in the left hand; yet he used this hand in writing, drawing, eating and other unimanual activities.

On March 19, although the weakness in the right hand persisted, he was able to write his name with it. He showed no evidence of visual agnosia or alexia in either homonymous field. Stereognosis was intact on both sides, but the patient showed tactile alexia in the right hand. He shuffled cards awkwardly but was able to light the examiner's cigaret with either hand, although he was awkward when using his right hand. Athetoid movements in this hand became more marked. Except for an increased right biceps reflex, the reflexes remained equal on the two sides.

On April 5 reflexes on the right side were exaggerated, but sensation was normal except for hyperesthesia and dysesthesia in the right arm. Palsy was present in the right lower side of the face. No evidence of tactile alexia was noted on either side. He was able to write with either hand with the eyes open or closed.

On April 12 the reflexes were equal, but the weakness of the right lower side of the face persisted. Sensory examination revealed hyperesthesia to pinprick and loss of vibration sense over the right side. Two point discrimination was as follows:

	Right Hand	Left Hand
Finger tip	2.5 mm.	2.5 mm.
Palm	5.0 mm.	5.0 mm.
Dorsum	11.0 mm.	11.0 mm.

Tactile lexia and stereognosis were intact on both sides.

On discharge, April 17, 1940, he still showed weakness in the right hand but was able to write his name, a dictated sentence and spontaneous words with the eyes open or closed. The Binet level had declined to 9 years 3 months, and the intelligence quotient was 71.

Subsequent Course.—He showed steady improvement at home, and the parents observed that he was more congenial and reasonable in his behavior. The terror attacks continued, however, but were less frequent. In June 1940 the attacks became more frequent, and he became apathetic and confused.

He was readmitted to the hospital on June 11 for study and was discharged July 4, 1940. Throughout his stay psychomotor retardation and moderate dysarthria were present; he was apathetic and at times confused. He continued to have terror seizures, usually at night. Because of these seizures the neurologic status was apt to vary from day to day. Palsy of the right lower side of the face was constantly present; the deep reflexes on the right were apt to be increased immediately after an attack, and a bilateral Babinski sign was occasionally found. Strength in the right hand was less than that in the left hand. The right arm showed usually an increase in muscle tonus, and occasional pseudoathetoid movements were observed. There was definite dyspraxia, and finer movements and diadokokinesis could not be performed with the right hand. With the eyes open he was able to write to dictation and spontaneously fairly well with the right hand but made several mistakes in spelling words, such as "pretty," "horse" and "Dukelow," his middle name. With the eyes closed he was unable to write with a pencil in his right hand because he had no appreciation of the position of his hand in relation to the paper. With his left hand he was able to write to dictation and spontaneously with the eyes open or closed. With the eyes open he could draw with his right hand such objects as a cat, a man, a house and tree or a cube fairly well, but these productions were inferior to his drawings before operation. Sensory disturbances, including hypesthesia and loss of vibration, position and localization senses over the right side, were usually present. However, the findings on sensory examination were apt to fluctuate considerably. The psychiatric status was changed from the preoperative state. He was dull; responses were delayed, and the attention-gaining behavior so characteristic before operation was absent. He showed defects in sensorium, mental capacity and intellect.

He was again studied in the hospital from March 17 to 27, 1941. The mother remarked on his marked improvement in behavior. He had become a docile, even-tempered lad. Since a grand mal seizure in January 1941, in which he fell down a flight of stairs, he had had a stutter, the degree of which was variable. Throughout this stay in the hospital he conducted himself in a cooperative and congenial manner. A formal psychiatric examination showed slight improvement over the findings one year before. The Binet level was 10 years and the intelligence quotient 72. The neurologic status revealed bilaterally equal deep

reflexes, equal strength of the hand grips (20 Kg.), an infrequent extensor response of the big toe on the left side, marked adiadokokinesis in the right hand and impairment of spatial localization and two point discrimination over the right hand. Stereognosis for fair-sized objects was intact. He was able to write with either hand with the eyes open or closed, and once again he was fairly proficient at drawing with his right hand. No evidence of dyspraxia was evident in either hand.

CASE 18.—G. E., a white farmer aged 35, was admitted to the Strong Memorial Hospital on May 2, 1940. In childhood he stuttered, but this disappeared in adolescence. At the age of 14 he had poliomyelitis, with residual weakness of the right leg. In 1933 osteomyelitis of the right tibia and lower part of the right femur developed. In August 1937 convulsions and right-sided paralysis, with an emissive form of aphasia, developed. On Sept. 3, 1937 an abscess in the left frontal lobe of the brain, beneath an area of osteomyelitis of the skull, was drained. The hemiplegia cleared up almost completely except for slight weakness. Speech returned, but he had a return of the stutter and noticed occasional difficulty in thinking of the proper word when writing or talking. The grand mal seizures continued, associated with an aura of a feeling that "something was going to happen." In the seizure the right arm thrashed about more than the left. After each attack he was aphasic for a variable period, and the right arm was paralyzed and numb for six hours or more. Petit mal attacks occurred at least once a day. The osteomyelitis in the right leg progressed, and in 1938 a midthigh amputation was performed. He was an extremely affable, cooperative man, of normal intelligence.

Physical status was good except for the amputated stump of the right thigh. Neurologic examination revealed exaggeration of deep tendon reflexes and a questionable Hoffmann reflex on the right side. Strength was equal in the two hands. The results of sensory examination were normal. Two point discrimination was as follows:

	Right Hand	Left Hand
Finger tip	3.5 mm.	3.0 mm.
Palm	9.0 mm.	10.0 mm.
Dorsum	23.0 mm.	29.0 mm.

He showed a speech disorder, most evident when he was tired or excited; it consisted of a stutter and a mild emissive form of aphasia. He noticed difficulty at times in spelling simple words while writing, and when asked to write the alphabet he had difficulty with t, u, v and z. He was able to write with either hand. (He remarked that when he was aphasic three years ago he had been unable to write with his left hand.) Electroencephalographic studies revealed delta waves in all leads, but they were of greatest amplitude over the left frontal region. Hyperventilation produced single petit mal–like waves in the left frontal region only. A ventriculogram showed a number of local dilatations of the ventricular system, most marked on the left side, and a shift of the pineal body to the left. Laterality studies revealed right ocular dominance and right handedness. Before amputation he was certain he used his right foot in kicking. Left cerebral dominance was well illustrated by the aphasic disorder associated with the right hemiplegia three years ago.

Operation.—On May 17, 1940 a midline frontal incision was carried out along the former incision and extended into the right temporal region. A new sheet of bone 3 to 4 mm. thick had formed over the area of previous bone removal. The right frontal lobe was easily retracted from the falx, and the corpus callo-

sum was sectioned completely. A scar approximately 2 cm. in diameter was found over the right superior frontal gyrus, or area 8 of Brodmann (fig. 4).

Course.—The postoperative course was uneventful. Dyspraxia was not noted in either hand.

On June 5, 1940 a detailed neurologic and psychiatric study was made. Except for an increased biceps reflex on the right side, the deep tendon reflexes were active and equal on the two sides. The strength as tested with the dynamometer was equal in the two hands. Sensation was normal, and two point discrimination was as follows:

	Right Hand	Left Hand
Finger tip	4 mm.	4 mm.
Palm	9 mm.	9 mm.
Dorsum	22 mm.	22 mm.

Stereognosis and tactile lexia were intact in both hands. A detailed study of praxia was performed, with no evidence of dyspraxia in either hand. He was able to write with either hand his name, a dictated and a spontaneous sentence with his eyes open or closed.

He was discharged on June 23, 1940 and has not been examined since. He had no difficulty in using his crutches. The stutter and dysphasia remained unchanged.

Group 1.—Cases in Which Motor Aspects of the Neurologic Status Were Normal Before and After Operation (10 cases).—In this group, consisting of 7 cases with partial section of the corpus callosum, 1 case with partial and subsequently complete section and 2 cases with complete section of the corpus callosum, no evidence of dyspraxia in the subordinate hand was observed postoperatively. The majority of this group showed some variable weakness in the hand contralateral to the craniotomy for a short period (from one to five days) immediately after operation. This paresis may have been due to several factors. Undoubtedly, retraction of the hemisphere in order to allow exposure and sectioning of the corpus callosum might result in some trauma. A second factor is the effect of anoxemia resulting from the ligation of occasional veins entering the longitudinal sinus in its anterior third if retrograde thrombosis into motor areas should occur. A third factor is related to the seizures which may occur shortly after operation as a result of abrupt hydration of the brain from intravenous administration of fluids during operation, as well as the withdrawal, in most instances, of anticonvulsant drugs during the stay in the hospital. These seizures are probably associated with vascular changes, which result in further anoxemia of parenchyma the blood supply of which is, or is likely to be, easily disturbed. In most cases in which craniotomy was done on the right side, paresis was noted in the subordinate, or left, hand. In case 6, in which the left frontoparietal lobe was exposed, paresis of the right side was observed after operation. The possibility of the removal of the inhibitory influences from the intact hemisphere on the damaged hemisphere should be considered also.

The argument has been advanced by Lange [3] that after partial surgical sectioning of the corpus callosum in which the genu and the body are cut, the secondary pathways from the supramarginal and angular gyri of the dominant hemisphere passing through the splenium to the "eupractic" center of Liepmann in the subordinate hemisphere escape and thus allow the praxic functions in the subordinate hand to remain undisturbed. This explanation is not tenable in view of the observations in those cases (8, 9 and 10) in which the corpus callosum was completely sectioned.

The question of the age of the patients must next be considered. The patients with sympathetic dyspraxia whose cases are described in the literature have been advanced in years. In the present group the average age was 25.7 years, the youngest being 16 and the oldest 43 years. Liepmann [21] remarked on the earlier recoverability from apraxia of younger patients. Sympathetic dyspraxia in cases of the syndrome of the anterior cerebral artery has been known to clear in six weeks. It may be contended that the subordinate hemisphere may quickly relearn the patterns of complex movements and thus the dyspraxia may be very transient and may be overlooked. This argument can be answered by the observations in cases 6 and 7. In case 6 the patient (ambidextrous) was able to draw with either hand twenty-four hours after operation. In cases 4 and 7 both patients (definitely right handed) showed no dyspraxia and were able to write with either hand forty-eight hours after operation.

The only consistent postoperative disturbance in these cases was dysdiadokokinesis. This was variable but persistent and involved the subordinate hand. In a case of partial agenesis of the corpus callosum in which the neurologic status was otherwise normal we have observed the same phenomenon.

In conclusion, it seems apparent that partial or complete section of the corpus callosum when uncomplicated by severe cerebral damage does not result in dyspraxia in either hand.

Group 2.—Cases in Which the Motor Aspects of the Neurologic Status were Normal Before Operation but Presented Postoperative Evidence of Cerebral Damage (3 cases).—In this group of 3 cases, 2 with partial section and 1 with partial and subsequently complete section of the corpus callosum, a kinetic form of dyspraxia in the subordinate hand occurred. In case 11 left hemiparesis and dysesthesias developed in the left hand after the first operation. Reelevation of the bone flap on the fifth postoperative day revealed retrograde thrombosis of a large ligated vein, which extended down toward the portion of the motor cortex concerned with arm movements. The dyspraxia was considered to be due to ataxia and paresis. There was no evidence of inversion of

21. Liepmann, H.: Apraxie, Ergebn. d. ges. Med. **1**:516, 1920.

movement of the type of mirror writing seen in cases of "sympathetic" dyspraxia, as described by Ingham.[22]

In case 12 the patient showed no difficulty in performing movements with his left hand until three days after operation, when difficulty in carrying out commands requiring finer movements was observed in the left hand. Death occurred on the tenth postoperative day. The autopsy observation of a subdural hematoma over the right frontal lobe explains the dyspraxia in the subordinate hand. This case is also remarkable in that with partial destruction of the parieto-occipital region of the "dominant," or left, hemisphere the patient exhibited no evidence of an ideokinetic form of apraxia (fig. 3 *B*).

In analyzing case 13 psychobiologic as well as neurogenic factors must be considered. The neurogenic factor consisted of definite clinical evidence of damage to the right cerebrum following the first operation and Erb's palsy of the left arm, which had been present since birth. These factors would adequately explain the dyspraxia in the left hand. Psychobiologic involvement, however, aggravated the picture to some extent. The very intelligent and sensitive woman in this case, who was preoccupied with her epilepsy and the fear that dementia paralytica might develop, became panicky and depressed when the hemiparesis and dysesthesias occurred postoperatively. The development of these disturbances was interpreted by the patient as a realization of her constant fear of dementia paralytica. Added to this fear was the discouragement she experienced when the attacks returned in their preoperative form. It is on this emotional basis that the decline in mental ability and the excessive "catastrophe" reactions may be ascribed in large part.

In conclusion, the kinetic form of dyspraxia arising in this group is a result of paresis. The origin of the paresis was on the basis of damage to the central nervous system. The close relation between motor paresis and dyspraxia has been commented on by Sittig,[23] Wilson,[15] Goldstein,[24] Herzog [25] and others.

Group 3.—Cases in Which Evidence of Cerebral Damage (Diffuse or Focal) Was Present Before Operation (5 cases).—In this group of 5 cases in which evidence of diffuse or focal involvement of the central nervous system was present before operation dyspraxia was absent in only 1 (case 18).

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22. Ingham, S. D.: Apraxia, California & West. Med. **45**:229, 1936.

23. Sittig, O.: Ueber Apraxie: Eine klinische Studie, Sonderausgabe von Heft 62 der Abhandlungen aus der Neurologie, Psychiatrie, Psychologie und ihren Grenzgebieten, Berlin, S. Karger, 1931.

24. Goldstein, K.: Zur Lehre von der motorischen Apraxie, J. f. Psychol. u. Neurol. **11**:169 and 270, 1908.

25. Herzog: Casuistischer Beitrag zur Lehre von der motorischen Apraxie, Ztschr. f. klin. Med. **53**:332, 1904.

Of the 2 cases in which the corpus callosum was partially sectioned, a focal lesion was present in 1 (case 14) and Pick's atrophy, with diffuse changes in the brain, in the other (case 15).

Case 14 had two interesting features. First, the patient was predominantly left brained until the age of 3, when right hemiplegia with aphasia developed. After this cerebral dominance probably shifted to the right hemisphere. At the time of operation she was left handed and showed mild residua of right hemiplegia. Second, there developed forced innervation in the right hand, with increased disturbance in the performance of skilled movements in this hand for about one month after operation. It is highly doubtful whether this forced innervation and the temporary increase of the dyspraxia were due to damage to the left cerebral hemisphere at the operation, since the craniotomy was performed on the right side. Astereognosis developed in the right hand, even though two point discrimination and interpretation of skin writing were not disturbed. This suggests that the astereognosis might be a result of the impaired manipulation of the object in the right hand; yet astereognosis has remained eight months after operation, even though the praxic functions in this hand have returned to their preoperative state. The dyspraxia was more in the nature of an increase in the ataxia present before operation and was temporary.

In case 15 there was evidence of left cerebral dominance for language functions, with the temporary occurrence of aphasia and right hemiplegia following a series of right-sided jacksonian seizures during convalescence. In all probability, the patient sustained added injury to the right cerebral hemisphere, since he showed marked hemiparesis temporarily after operation. Although incapable of waving goodby or touching his nose with his left hand on request, he could easily rub his nose or scratch his neck with this hand spontaneously. This suggests that there was a distinct dissociation between voluntary and instinctive, or primitive, actions in the left hand. Subsequently, he showed temporary dyspraxia of an ideokinetic type, such as was noted in the striking of a match on a paper cover. The tendency to confusion and "catastrophe" reactions whenever the left side was tested is probably best explained on the basis of psychobiologic factors. This man was apprehensive and probably much concerned over the difficulties he noticed on his left side, and he became panicky and confused whenever the examiner wished to study functions on this side. In contrast to the indifference of apraxic patients to their errors, as mentioned by Wilson [15] and others, this patient was almost hypochondriacal in his concern. In brief, he showed evidence of an ideokinetic type of dyspraxia in the left hand after operation, which subsequently cleared. The ability to perform learned movements with the left hand, such as take place in eating and drinking, during the period in which he was aphasic and paralyzed on the right side suggests the possibility that the subordinate hemisphere is capable of utilizing the

engrams for this type of behavior even though the connections (secondary) with the supramarginal and angular gyri of the dominant hemisphere by means of the corpus callosum have been destroyed. This observation is contradictory to the observations of several investigators. In right-handed subjects left-sided apraxia was coexistent with right-sided hemiplegia, as described by Liepmann and Maas,[2] Rose and Touchard,[26] Vix,[27] Claude,[28] von Rad,[29] Claude and Loyez,[30] Foix [31] (case 1) and von Stauffenberg [32] (case 8). In left-handed subjects right-sided apraxia associated with left hemiplegia has been reported by Rothmann [33] and Taterka.[34]

Of the 3 cases in group 3 with complete section of the corpus callosum, definite dyspraxia in the subordinate hand was present on admission in 1 (case 16).

In case 16 the patient had sufficient dyspraxia in her left hand as a result of old left hemiplegia to make it impossible for her to learn to play the piano or to typewrite. She showed accentuation of this kinetic form of dyspraxia and suggestive ideokinetic dyspraxia after operation. This was associated with forced motor innervation, astereognosis and sensory disturbances in the left hand. No veins were ligated at operation. According to Van Wagenen, these changes and the exaggerated dyspraxia in the subordinate hand are considered to be due to cutting of collateral fibers from the dominant hemisphere to the less dominant, and in this instance the old damaged, hemisphere. These collateral fibers may serve in a measure to control certain functions in the less dominant

26. Rose, F., and Touchard, P.: Hémiplégie droite et apraxie gauche, Rev. neurol. **17**:591, 1909.

27. Vix: Anatomischer Befund zu dem in Band 37 dieses Archivs veröffentlichen Fall von transkortikaler sensorischer Aphasie, Arch. f. Psychiat. **47**:200, 1910. This is an anatomic study of a case reported by Bonhoeffer (Kasuistischen Beiträge zur Aphasielehre, ibid. **37**:800, 1903).

28. Claude, H.: Sur un cas d'hémiplégie droite avec apraxie du membre supérieur gauche. Phénomènes d'akinésie, Rev. neurol. **19**:329, 1910.

29. von Rad: Ueber Apraxie bei Balkendurchtrennung, Ztschr. f. d. ges. Neurol. u. Psychiat. **20**:533, 1913.

30. Claude, H., and Loyez, M.: Etude anatomique d'un cas d'apraxie avec hémiplégie droite et cécité verbale, Encéphale **8**:289, 1913.

31. Foix, C.: Contribution à l'étude de l'apraxie idéo-motrice, de son anatomie pathologique et de ses rapports avec les syndromes qui ordinairement l'accompagnent, Rev. neurol. **29**:280, 1916.

32. von Stauffenberg: Klinische und anatomische Beiträge zur Kenntnis der aphasischen, agnostischen und apraktischen Symptome, Ztschr. f. d. ges. Neurol. u. Psychiat. **39**:71, 1918.

33. Rothmann, M.: Apraxie der rechten Hand bei linksseitiger Hemiplegie beim Linkshänder, Deutsche Ztschr. f. Nervenh. **41**:271, 1911.

34. Taterka, H.: Partielle Apraxie des rechten Armes nach linksseitiger Hemiplegie bei einer Linkshänderen, Ztschr. f. d. ges. Neurol. u. Psychiat. **90**: 573, 1924.

hemisphere. After section of these collaterals, the less dominant hemisphere usually reassumes the functions it possessed prior to operation and does so in a few weeks. Operative trauma and retrograde venous thrombosis cannot be invoked to satisfy all of the postoperative phenomena, and probably account for few of them. To one of us (Akelaitis), however, the hypesthesia, including disturbance of two point discrimination and accentuation of the motor aspects of the hemiplegia after operation, suggests strongly the possibility of added injury to the right hemisphere of the cerebrum.

In case 17 the patient showed evidence of diffuse cortical involvement with fluctuating neurologic signs before operation. After section of the corpus callosum the frequent occurrence of "terror" attacks produced further complications in the already fluctuating picture, such as the temporary right hemiparesis with sensory disturbances on the right side. The fact that the right frontoparietal lobe was exposed at operation suggests that the neurologic changes on the right side were not related to operative trauma.

The absence of postoperative changes in case 18 is surprising, since a small scar was present over the right superior frontal gyrus and since scarring over the left frontal lobe probably was even greater. The continuation of the stutter after complete section of the corpus callosum would cast doubt on the theory that speech disorders are caused by conflicts between the two hemispheres, neither of which has achieved dominance in language function insofar as these conflicts are mediated through the fibers of the corpus callosum.

In this group a temporary form of ideokinetic dyspraxia in the subordinate hand was found in 2 instances (cases 15 and 16). In case 15 diffuse atrophy of the brain was present. According to Van Wagenen, operative trauma to the right cerebral hemisphere is always possible, but is improbable in this case. However, in the opinion of one of us (Akelaitis), the hemiparesis and transient appearance of a Babinski sign on the left side are evidence of added injury to the right cerebral hemisphere. In case 16 focal atrophy of the right cerebral hemisphere was present before operation, and it is uncertain whether this hemisphere suffered further damage. In case 17 so many fluctuations occurred in the neurologic status associated with seizures that it is quite impossible to evaluate the role of section of the corpus callosum alone. In case 18 no changes occurred. We are all agreed that case 14 is the only one in which an exaggeration of the kinetic dyspraxia present before operation could be reasonably related to the section of the corpus callosum.

COMMENT

The absence of dyspraxia in either hand in all of the cases of group 1 and in case 18 of group 3 requires the consideration of various possibilities for an adequate interpretation. These possibilities will be

analyzed as follows: (1) the representation of praxic functions in each of the two hemispheres; (2) utilization of other, subcortical commissural pathways, and (3) ipsilateral representation of motor functions in the dominant hemisphere.

1. *Representation of Praxic Functions in Each of the Two Hemispheres.*—The concept of a unilateral cerebral dominance began with the theory of Dax [35] and was extended by the studies of Broca, Charcot, Wernicke and others. On this basis, as formulated by Hughlings Jackson and subsequent workers, the subordinate (usually right) hemisphere was capable of automatic, or primitive, activities, in contrast to the dominant hemisphere, which represented voluntary activity. In recent years, however, the importance of the subordinate hemisphere as being capable of reaching a considerably higher development than was supposed to be possible in the past has been emphasized. Even in respect to language function, in which manifestations of unilateral cerebral dominance have been most marked, cases have been reported which suggest that the subordinate, or minor, hemisphere can take on the functions of speech (Kuttner,[36] Lovell and associates,[37] Singer and Low,[38] Zollinger,[39] Wechsler,[40] Fox and German,[41] and Nielsen and Raney [42]). In children the speech area in the dominant hemisphere is not well established and may be transferred to a large degree to the subordinate hemisphere, as seen in case 14. At present the idea is gaining ground that the degree of unilateral dominance is variable among different persons. Consequently, two factors must be considered in relation to the patients in this series. First, the relative youthfulness of these patients may account for the ease with which the subordinate hand was able to take on praxic functions. Insofar as unilateral dominance for speech is concerned, transferability is difficult after the

35. Dax, M.: Lésions de la moitié gauche de l'encéphale coincident avec l'oubli des signes de la pensée, Montpellier, 1836.

36. Kuttner, H.: Ueber die Beteiligung der rechten Hirnhälfte an der Sprachfunktion. Kasuistische Mitteilung zum Aphasieproblem, Arch. f. Psychiat. **91:** 691, 1930.

37. Lovell, H. W.; Waggoner, R. W., and Kahn, E. A.: Critical Study of a Case of Aphasia, Arch. Neurol. & Psychiat. **28:**1178 (Nov.) 1932.

38. Singer, H. D., and Low, A. A.: The Brain in a Case of Motor Aphasia in Which Improvement Occurred with Training, Arch. Neurol. & Psychiat. **29:** 162 (Jan.) 1933.

39. Zollinger, R.: Removal of Left Cerebral Hemisphere, Arch. Neurol. & Psychiat. **34:**1055 (Nov.) 1935.

40. Wechsler, I. S.: The Excision of the Speech Area Without Resulting Aphasia, Arch. Neurol. & Psychiat. **38:**430 (Aug.) 1937.

41. Fox, J. C., Jr., and German, W. J.: Observations Following Left (Dominant) Temporal Lobectomy: Report of a Case, Arch. Neurol. & Psychiat. **33:** 791 (April) 1935.

42. Nielsen, J. M., and Raney, R. B.: Recovery from Aphasia Studied in Cases of Lobectomy, Arch. Neurol. & Psychiat. **42:**189 (Aug.) 1939.

age of 12, and, with the exception of case 14, the patients in all cases were above this age; it seems unlikely, therefore, that this factor could explain the results. A second consideration is the possibility that these patients exhibited a greater degree of mixed dominance than is found in the average population. No evidence for this was found in the series insofar as various tests for laterality functions can be used in the determination of cerebral dominance (Smith and Akelaitis [11]).

Cases 15 and 18 can be utilized to give further insight into this problem. With the development of a left frontoparietal abscess and resultant right hemiplegia, the patient in case 18 was unable to write with his left hand but was capable of using his left hand in eating, and although no formal tests for praxis were performed at this time, he apparently showed no notable dyspraxia. It is reasonable to say that ability to write is determined by the left hemisphere, but the problem of praxis is unsolved. It may reasonably be argued that the secondary pathways from the left parieto-occipitotemporal region through the corpus callosum to the arm center in the right hemisphere were capable of allowing praxis in the left hand. The patient in case 15 was able to use his left hand in eating during the interval when he had right hemiplegia and emissive aphasia. The corpus callosum was almost entirely sectioned in this patient, and consequently the secondary pathways for praxic engrams from the supramarginal and marginal gyri of the dominant hemisphere were destroyed. However, subcortical commissural pathways may have played a role here, although in the light of present knowledge we have no direct evidence for this assumption. In brief, therefore, suggestive but not conclusive evidence for representation of praxic functions residing in each hemisphere can be furnished from this study.

2. *Utilization of Subcortical Commissural Pathways.*—The recent work of Curtis [43] has demonstrated physiologically the long-accepted opinion that the corpus callosum constitutes the interhemispheral connections between homologous and, to a less extent, heterologous areas of the cerebral hemispheres. According to Mingazzini,[44] the genu contains fibers uniting the frontal lobes; the body is made up of fibers uniting, on the two sides, the first frontal and the precentral gyrus, the paracentral lobules and the insulas, and the fibers of the splenium unite the parietal, occipital and temporal lobes. Other commissural systems must be considered. In dogs interhemispheral fibers from the frontal lobes have been described in the septum pellucidum by Shukowski.[45]

43. Curtis, H. J.: Intercortical Connections of Corpus Callosum as Indicated by Evoked Potentials, J. Neurophysiol. **3**:407, 1940; An Analysis of Cortical Potentials Mediated by the Corpus Callosum, ibid. **3**:414, 1940.

44. Mingazzini, G.: Der Balken, Berlin, Julius Springer, 1922.

45. Shukowski, cited by Bekhterev, V. M.: Die Leitungsbahnen im Gehirn und Rückenmark, ed. 2, Leipzig, A. Georgi, 1899.

No evidence of such fibers has been found in man. The hippocampal commissure apparently is concerned entirely with fibers connecting the hippocampi. The anterior commissure in man consists of a small anterior portion, containing olfactory fibers, and a larger neopallial portion, which according to Dejerine [46] is made up of interhemispheral fibers from the anterior portions of the temporal lobes. The posterior commissure probably contains fibers concerned with associated movements of the eyes (Collier [47]). The fibers forming the habenular commissure and the commissures of Gudden and Meynert deal presumably with optic and olfactory functions. The massa intermedia is an inconstant structure and contains few myelinated fibers, according to Morel and Weissfeiler.[48] Forel's posterior subthalamic commissure is made up of the ansa lenticularis and interluysial fibers, and possibly other fibers concerned with interlenticular relations. There may be other commissural pathways in the midbrain, and even lower down in the central nervous system, which are utilized. In the light of present knowledge it would appear highly improbable that these commissural systems could take over the functions of the corpus callosum in such finely synchronous bilateral activities as playing a piano, as seen in cases 1, 2, 3, 6 and 13, and typing by means of the touch system, as noted in cases 2, 3, 4 and 13. Only in case 13 of this series was there a complete section of the corpus callosum. It must be emphasized that in typing with both hands by means of the touch system the subject is not allowed to look at the keyboard and has, therefore, to divide the words typed between the two hands. It might be argued that patient 13 had memorized the words she typed, but surely this contention falls down completely in view of the fact that she succeeded with the typing of sentences in a language she had no knowledge of.

3. *Ipsilateral Representation of Praxic Functions in the Dominant Hemisphere.*—Bucy and Fulton [49] observed ipsilateral responses in the extremities of monkeys by stimulation of area 6 of Brodmann, and Kennard and Watts [50] were able to elicit ipsilateral movements by stimulation of the same area in monkeys after complete section of the

46. Dejerine, J. J.: Anatomie des centres nerveux, Paris, Rueff & Cie, 1895, vol. 1.

47. Collier, J.: Nuclear Ophthalmoplegia, with Special Reference to Retraction of the Lids and Ptosis and to Lesions of the Posterior Commissure, Brain **50**:488, 1927.

48. Morel, F., and Weissfeiler, J.: La commissure grise. Etude anatomo-clinique, Encéphale **26**:659, 1931.

49. Bucy, P. C., and Fulton, J. J.: Ipsilateral Representation in the Motor and Premotor Cortex of Monkeys, Brain **56**:318, 1933.

50. Kennard, M. A., and Watts, J. W.: The Effect of Section of the Corpus Callosum on the Motor Performance of Monkeys, J. Nerv. & Ment. Dis. **79**: 159, 1934.

corpus callosum. Bucy and Fulton [49] referred to clinical material which they believed was suggestive of ipsilateral motor representation in the cerebral cortex of man. Foerster,[51] on faradic stimulation of the leg area in cases of internal hydrocephalus, was able to elicit movements in the ipsilateral leg before and after partial section of the corpus callosum. He observed bilateral movements of the legs on stimulation of the leg area of the intact hemisphere in cases in which the leg area in the opposite hemisphere was destroyed. Penfield and Boldrey,[52] as a result of cortical stimulations in more than 100 cases, concluded that "ipsilateral response practically does not exist for motor movements."

It is common knowledge among neurologists that in hemiplegic patients paralysis is greatest in the distal portions of the arm and that in patients who have almost complete destruction of one hemisphere, movements at the contralateral shoulder may be performed fairly well although the fingers cannot be moved voluntarily. This peculiar distribution of paralysis following severe injury to the motor cortex or the internal capsule was first described by Wernicke.[53] This suggests either that the distal portions have a much poorer ipsilateral representation in the brain or that the restitution of function in the distal portions is very poor, due to the greater vulnerability of the area in the contralateral hemisphere. Early in the postoperative course the patient in case 16 was unable to write with a pencil in her left hand but had no difficulty in performing writing movements at the left shoulder. Another epileptic patient not reported on in the present study had severe right-sided cerebral palsy. At operation the corpus callosum was completely divided and the left hemisphere was found to be replaced by a cyst. After operation he was able to write in the air by movements at the right shoulder with the eyes closed.

It is thus impossible to explain the findings in this investigation on the basis of any one of the three possibilities discussed. It is probable that each plays a definite, but variable, role. At present further investigations by means of such procedures as transfer of maze learning from the right to the left hand (K. U. Smith) and the study of reaction time to various stimuli (Smith and Akelaitis) are being made in order to evaluate the relative importance of each of these possibilities.

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51. Foerster, O.: Motorische Felder und Bahnen, in Bumke, O., and Foerster, O.: Handbuch der Neurologie, Berlin, Julius Springer, 1936, vol. 6, pp. 1-357.

52. Penfield, W., and Boldrey, E.: Somatic Motor and Sensory Representation in the Cerebral Cortex of Man as Studied by Electrical Stimulation, Brain **60**:389, 1937.

53. Wernicke, C.: Zur Kenntniss der cerebralen Hemiplegie, Berl. klin. Wchnschr. **26**:969, 1889.

SUMMARY AND CONCLUSION

In 18 cases of epilepsy the corpus callosum was sectioned in variable degrees. The extent of the division varied from merely section of the body and the posterior half of the genu to complete section of the corpus callosum.

The first group was made up of 10 cases in which the motor aspects of the neurologic status were normal before and after operation. This group consisted of 7 cases with partial section, 1 case with partial and subsequently complete section and 2 cases with complete section. No dyspraxia in either hand was found after sectioning of the corpus callosum.

The second group consisted of 3 cases in which the motor aspects of the neurologic status, insofar as the central nervous system was concerned, were normal before operation but in which evidence of cerebral damage was presented postoperatively. This group was made up of 2 cases with partial section and 1 case with partial and subsequently complete section of the corpus callosum. In all 3 cases a kinetic type of dyspraxia was found. In all probability this dyspraxia was based on motor paresis and in 2 cases was associated with additional sensory changes.

The third group was composed of 5 cases with evidence of diffuse or focal changes in the central nervous system before operation. This group consisted of 2 cases with partial section and 3 cases with complete section. Dyspraxia was absent in only 1 case (18). In 2 cases (15 and 16) a temporary form of ideokinetic dyspraxia occurred in the subordinant hand, associated with forced innervation and sensory changes. We are not agreed as to the possibility of further damage to the subordinate hemisphere in both these cases. In another case (17) the kinetic dyspraxia in the dominant hand was associated with motor paresis and sensory disturbances. Case 14 is the only one in which an exaggeration of the kinetic dyspraxia evident before operation could be directly attributed to the partial section of the corpus callosum.

On the basis of this study the conclusion may be drawn that dyspraxia in the subordinate or dominant hand after partial or complete section of the corpus callosum occurs only when damage to the subordinate or dominant hemisphere coexists.

DISCUSSION

DR. J. M. NIELSEN, Los Angeles: This work of Dr. Akelaitis and his associates is a beautiful confirmation of what has long been supposed about apraxia. Of course, much water has gone over the dam since the time of Liepmann. It is no longer thought that one hemisphere is dominant over the other. It was the idea of dominance that gave rise to the concept of the right side being governed by the left. The relation of the two hemispheres is much more nearly that of pilot and copilot on an airplane. If they are connected with a rope they

will function, and if the rope is cut they will continue to function. An ideational plan is formed in the left hemisphere for the right side of the body and in the right hemisphere for the left side of the body. That can be demonstrated even without section of the corpus callosum. But each side governs the opposite side as far as acts are concerned. Only ideokinetic apraxia is under discussion here; Liepmann's so-called kinetic apraxia of the limb has nothing to do with the corpus callosum, nor does ideational apraxia. The splenium of the corpus callosum is not concerned with apraxia, anyway, but with agnosia.

As long ago as 1914, and subsequently, von Monakow, and later his pupil Bruns, showed that apraxia never persists unless the lesion is a progressive one. One sees literally hundreds of cases of thrombosis of the left middle cerebral artery with pronounced aphasia, but rarely does one see apraxia. If the left side and of course the fibers of the corpus callosum are thrown out of function so completely with such a thrombosis, why is not apraxia produced? It is because the ideational plan for the other side of the body is formed on the other side of the brain. So it seems to me that everything presented here is entirely confirmatory and that the reason Dr. Akelaitis found the dyspraxia when the minor side was involved was that this side, now having to work entirely independently, was simply not capable of it; for most acts, however, the two sides of the brain work entirely separately. The discussion of language function is another matter, and I think I had better not even touch on that.

Dr. Leo M. Davidoff, New York: About seven years ago Dr. Dyke and I had the opportunity to check by postmortem examination the peculiar appearance of an encephalogram and were able to confirm the diagnosis of congenital absence of the corpus callosum. Since then we have seen at least half a dozen cases in which we were able to make such a diagnosis and to study the dyspraxias involved. We were able to confirm the observations that were reported here.

It is of interest that 1 of these cases, one of the few in which the patient, an adult, was perfectly normal except for the presence of epilepsy, provided the opportunity to confirm the diagnosis by an exploration, which was done by Dr. Van Wagenen.

Dr. Andrew J. Akelaitis, Rochester, N. Y.: It is interesting that in the case Dr. Davidoff described the only neurologic disturbance that we could pick up was adiadokokinesis on the left side. That was before the exploratory craniotomy. Interestingly, almost all of the patients in our series showed the same type of disturbance after operation; in fact, that is about the only neurologic sign that one could find fairly consistently.

Now, regarding the idea that the two hemispheres work independently, I feel that such activities as the ability to typewrite, in which the subject divides the word between the two hands, is rather conclusive proof that one is dealing with subcallosal commissural fibers. I should like to add that further studies are being made, especially by Dr. Karl U. Smith, of the department of psychology of the University of Rochester, on the transfer of learning from the dominant to the subordinate hand. It is surprising how quickly and how well these patients can utilize the learning in the right hand and transfer it to the left hand.

Dr. Smith and I are carrying out investigations on the reaction time to rather complicated and to simple stimuli. This work suggests that when the corpus callosum is cut the functional connections between the two hemispheres are not destroyed to any large degree.

DISTURBANCES IN BRAIN FUNCTION FOLLOWING CONVULSIVE SHOCK THERAPY

ELECTROENCEPHALOGRAPHIC AND CLINICAL STUDIES

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As a result of the recent widespread use of convulsive shock therapy for psychiatric disorders, the effect of this treatment on the structure and function of the brain has become a matter of considerable concern to clinicians. This has been augmented since convulsive shock therapy has been successfully employed to shorten attacks of affective disorders in which intellectual functions are maintained and emerge undisturbed with spontaneous recovery.

MATERIAL AND METHODS

Patients under the regimen of convulsive therapy were studied neurologically and psychiatrically before and after treatment. Electroencephalograms were recorded before the first shock and at varying times after cessation of the treatment; some patients were completely rechecked at intervals several months after discharge from the hospital. Such studies were carried out on 23 patients, all but 4 of whom were suffering from primary or secondary affective disorders (see table 1 for significant data). Of the 4 other patients, 2 were schizophrenic, 1 was paranoid with depression and 1 was schizophrenic with no significant disturbance in mood. All the patients were free from evidences of neurologic disease. Evidence of sensorial and intellectual disturbances of the "organic" type was absent in all cases before treatment.

The technic of the electroencephalographic examination consisted of "global" recordings of brain potentials from the two hemispheres, bipolar lead pellet leads fastened only over the premotor and occipital areas being used. The amplifiers were of the usual push-pull resistance-capacity–coupled type. Recording was done by means of an ink writing crystograph.

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Therapy consisted of metrazol-induced convulsions in 11 patients and electrically induced convulsions in 12 patients. Relatively small numbers of treatments were used, the maximum being eleven. The customary technic of intravenous administration of metrazol was employed, no other drug being used in conjunction with the metrazol. As a rule a treatment was given every other day, but in some instances the interval between treatments was longer.

Inasmuch as electric shock therapy has been described in only a few publications in the American literature (Kalinowsky and Barrera), our technic will be given in some detail. Treatments were administered every other day. No sedation was given during the preceding night, and breakfast was withheld until after the treatment. During the convulsive seizure care was taken to prevent violent body movements. With the patient on a rigid bed, corresponding areas of the scalp over the premotor regions were rubbed with a standard electrode jelly and covered with pads moistened with saline solution. Two German silver electrodes, 2.5 cm. square, were fastened over the pads with an adjustable elastic band. Unlike the technic originally used by Cerletti and Bini, no measurements of direct current resistance were made. Instead, a small percentage of the final alternating current was passed through the head as a "test" current. With the aid of a variable transformer, the desired milliamperage reading could be obtained as the patient's resistance was automatically taken into account. The reading on the test meter corresponded with that on the treatment meter. This type of apparatus was found preferable to the original one used by Cerletti, since it had been noted that the observed alternating current passed through a polarizable tissue was higher than that calculated by Ohm's law when the direct current resistance and voltage alone were known. An electronic timer was used, thus making possible accurate current-time relations, the primarily important factors in the stimulation of biologic tissues. With the usual setting of 300 to 500 milliamperes and passage of the current for two to five tenths of a second, a convulsion occurred within thirty seconds after the treatment switch was closed. In the event of failure ("petit mal reaction") following passage of the current, the resultant increase in transcerebral conduction at once necessitated a new test current setting and a second treatment current. Amnesia for the treatment eventuated in either case. Safety devices on the apparatus included, in addition to the manual operation of the keys, a circuit breaker of variable setting and an automatic "interlocking" of the two circuits so that treatment could not be administered until a "test" current had been employed. After a convulsion consciousness was regained in twenty to thirty minutes, with considerably less agitation and confusion than with metrazol therapy, and patients were allowed out of bed in two or three hours. The amnesia usually diminished by evening. In contrast to metrazol treatment, because of the rapidity of loss of consciousness and the amnesia, patients subjected to electric shock convulsions do not as a rule show fear of the treatment.

In addition to the convulsive treatment, varying amounts and types of psychotherapy were given, and the customary psychiatric regimen, occupational therapy, hydrotherapy and medication were instituted. In the majority of cases psychotherapy was limited to the supportive, reassuring type. In certain cases more intensive therapy directed at uncovering emotional conflicts and deeper sources of anxiety was utilized.

RESULTS OF SHOCK THERAPY

Clinical Observations.—The results of therapy were recorded according to the three categories, "recovered," "improved" and "unimproved." Recovery indicates a return to the premorbid status, with adjustment and absence of symptoms. The patient was considered improved when there was considerable objective and subjective amelioration of the symptoms. The patient whose condition became worse, remained unchanged or showed slight symptomatic improvement was classified as unimproved. Similarly, the patient who showed improvement but whose symptoms recurred within several weeks or a few months was considered unimproved.

The results of treatment were as follows: In the metrazol series (11 patients) 4 recovered (patients 4, 5, 8 and 10), 1 improved (patient 6) and 6 did not improve (patients 1, 2, 3, 7, 9 and 11). In the electrically treated series (12 patients) 7 recovered (patients 13, 14, 15, 16, 17, 21 and 22), 2 improved (patients 12 and 19) and 3 showed no improvement (patients 18, 20 and 23). Of the whole series, 14 recovered or improved and 9 did not improve. From these data it would appear that in this small series of patients better therapeutic results were achieved with electrically induced than with metrazol-induced convulsions. The types of patients in the two series were reasonably comparable, except that there were 2 schizophrenic patients in the metrazol series and only 1 in the electric shock series. With these exceptions, the patients all had either primary affective disorders or depressive reactions as part of a neurosis, and 1 had a depressive reaction in a paranoid state. Of the 3 schizophrenic patients, however, 2 had depressive mood reactions. From the results with this material, and from our experience in cases not included in this report, it is our impression that the primary affective disorders respond best to convulsive shock therapy. The type of depressive reaction which occurs so frequently in persons with a chronic neurosis, especially the thwarted infantile, dependent personality, seems definitely to respond less well and to recur much more easily. The most striking feature of convulsive therapy of these affective disorders is not the incidence but the dramatic rapidity of recovery. Depressive conditions which formerly would persist from six months to a year or two with the best psychiatric management spectacularly recover in the course of several weeks.

Neurologic Observations.—Examination by the usual neurologic technic was carried out after the course of shock therapy had been completed, in most instances at least several days after the last treatment. The results of examination were uniformly negative, no objective evidence of organic disturbance of the nervous system being encountered,

Clinical and Electroencephalographic Data

Case No.; Name	Date of Admission	Sex	Age, Yr.	Clinical Diagnosis	Duration of Illness	Number and Type of Treatments	Clinical Result	Pretherapy Electroencephalogram	Posttherapy Electroencephalogram	Posttherapy Intellectual Function
1 L. S.	March 1940	F	42	Neurotic depression; infantile dependent personality	2 mo.	3; metrazol	No improvement	Normal curve with normal alpha waves	No change	No impairment
2 A. A.	March 1940	F	52	Agitated depression	Months	7; metrazol	Progression of psychosis	Normal curve; fair alpha rhythm; beta rhythm indicated, not clear	Occasional run of alpha rhythm; 3 per sec. waves; random activity; increased beta activity	Not determined because of severity of psychosis
3 N. G.	March 1940	F	20	Depression	Months	2; metrazol	Slight improvement	Normal curve with normal alpha rhythm	Slightly higher amplitude in alpha waves	No impairment
4 G. N.	March 1940	F	44	Depression	3 mo.	2; metrazol	Hypomanic phase followed by recovery; follow-up January 1941, well and working	Not obtained	No alpha activity; 18 per sec. waves	Severe impairment for several weeks; patient "slap-happy"
5 J. W.	April 1940	M	52	Reactive depression	2 mo.	3; metrazol	Recovery; follow-up January 1941, well and working	Normal curve with normal alpha rhythm	Diminution of alpha waves; increased rapid activity	No impairment
6 S. R.	May 1940	F	42	Paranoid depression	Indefinite	4; metrazol	Depression improved	Normal curve	No change except for slight increase in beta activity	No impairment
7 F. K.	May 1940	F	47	Anxiety depression	1 yr.	5; metrazol	Improvement; recurrence in several weeks	Some irregularity; alpha rhythm good in places; maximum amplitude 50 mv.; some small bicuspid waves	Epileptoid curve, consisting of 6 and 3 per sec. waves, suggestive spike-curve formations; increased amplitude, up to 125 mv.	No impairment
8 E. W.	April 1940	F	32	Neurotic depression; infantile dependent personality	2 mo.	2; metrazol	Recovery; follow-up August 1940, well	Some random activity	Alpha rhythm and fewer delta waves	No impairment
9 H. P.	July 1940	F	34	Depression in schizophrenia	5 mo.	3; metrazol	Further regression	Fairly regular alpha rhythm; maximum amplitude 100 mv.	Epileptoid curve, with 6 per sec. waves predominating, notched waves and increased amplitude, up to 200 mv.	Not determined because of regressed state
10 R. S.	May 1940	F	51	Depression	18 mo.	5; metrazol	Manic phase, followed by recovery; follow-up December 1940—well, working, no complaints	Normal curve; maximum alpha rhythm 60 mv.	Epileptoid curve, with 3 per sec. waves, spike and wave formation, increased amplitude up to 210 mv. Electroencephalogram (Dec. 1940): regular alpha rhythm, with highest amplitude 100 mv., occasional series of 4 per sec. waves, no 3 per sec. waves, no spike and wave formations	Severe impairment; "slap-happy"; reexamination December 1940; still slight intellectual slowing
11 L. T.	February 1938	M	18	Schizophrenia	1 wk.	9; metrazol	Slight improvement	Normal curve	Epileptoid curve, with 3 and 6 per sec. waves	Not recorded
12 J. T.	March 1940	F	30	Anxiety depression in severe obsessive compulsive neurosis with conversion symptoms	3 yr.	8; electric shock	Improvement in depression and conversion symptoms; no change in underlying obsessive-compulsive neurosis	Rare alpha waves; many beta waves; some delta activity	Better alpha waves; fewer delta waves	Marked impairment for several weeks
13 M. S.	August 1940	M	40	Manic-depressive psychosis, depressed	2½ yr.	5; electric shock	Recovery	Some delta activity	Curve regular; increase in alpha rhythm; decrease in delta rhythm	No impairment
14 B. W.	November 1940	M	48	Depression	6 wk.	10; electric shock	No change	Slight	No change	No improvement
15 J. G.	November 1940	F	49	Recurrent depression	2 mo.	5; electric shock	Recovery; follow-up Jan. 1941—well, no complaints	Alpha waves of low amplitude, not measurable	Epileptoid curve, with 3 and 6 per sec. waves, increased amplitude, up to 80 mv. Electro-	Marked impairment for several weeks

13 M. S.	August 1940	M	40	Manic-depressive psychosis, depressed	2½ yr.	5; electric shock	Recovery	Some delta activity	Curve regular; increase in alpha rhythm; decrease in beta rhythm	No impairment
14 B. W.	August 1940	F	49	Recurrent depression	2 mo.	10; electric shock	Recovery	Normal	No change	No impairment
15 J. G.	November 1940	F	49	Recurrent depression	2 mo.	5; electric shock	Recovery; follow-up Jan. 1941—well, no complaints	Alpha waves of low amplitude, not measurable	Epileptoid curve, with 3 and 6 per sec. waves, increased amplitude, up to 80 mv. Electroencephalogram (Dec. 1940); curve normal even with hyperventilation, alpha waves 50 mv.	Marked impairment for several weeks
16 R. L.	December 1940	F	34	Recurring neurotic depressions during five year period	5 wk.	8; electric shock	Recovery from current depression	Normal	After 3d treatment, 3 and 6 per sec. waves, notched waves, questionable spike and wave formation, increased amplitude. After 8th treatment epileptoid curve; completely irregular, some alpha waves discernible, large 3 and 4 per sec. waves, with maximum amplitude up to 120 mv., notched plateaus, definite spike and waves	Marked impairment; "slap-happy"
17 F. P.	July 1940	F	36	Recurrent depression	3 mo.	4; electric shock	Manic phase, with recovery; follow-up Oct. 1940—well	Large quantity of beta waves; alpha rhythm present, not pronounced; much random activity	Normal alpha waves; fewer beta waves, and more regular curve	Impairment for several weeks; "slap-happy"
18 M. W.	July 1940	F	38	Neurotic depression	3 mo.	4; electric shock	Slight improvement	Normal	No change	No impairment
19 S. H.	September 1940	F	24	Depression in schizophrenia	1 yr.	11; electric shock	Depression; improvement	Normal	6 per sec. waves; questionable spike and wave formations	Severe impairment for several weeks
20 E. B.	November 1940	M	38	Depression	5 wk.	5; electric shock	Improvement; recurrence 1 mo. later	Normal	No change	Not determined
21 A. H.	September 1940	M	38	Manic-depressive psychosis, manic phase	3 mo.	8; electric shock	Recovery; follow-up Dec. 1940—well, working	Normal	No change	Severe impairment for several weeks
22 J. K.	October 1940	F	31	Neurotic depression; compulsive character	3 yr.	2; electric shock	Marked improvement; returned to work; follow-up Jan. 1941—no recurrence, working, apparently recovered	Low amplitude alpha rhythm	Epileptoid curve, with 3 and 6 per sec. waves. On hyperventilation, bicuspid waves, spike and wave formation; increased amplitude, up to 200 mv. Electroencephalogram (Dec. 8, 1940): fairly regular curve, with alpha activity of 35 mv. After hyperventilation, epileptoid curve, with irregular 4 per sec. waves, large 3 per sec. waves, with maximum amplitude of 150 mv. Return to normal in 12½ sec.	Moderate impairment; intellectual slowing; reexamination (Dec. 15, 1940): much improvement, but still some difficulty in intellectual performance
23 M. L.	August 1940	F	57	Neurotic depression with hypochondriasis	9 mo.	9; electric shock	Improvement, with rapid recurrence	No alpha waves; marked beta activity; some delta activity	Epileptoid curve, with 3 and 6 per sec. waves, dicrotic waves, spike and wave formation, increased amplitude, up to 200 mv., alpha waves of 9 per sec. Electroencephalogram (Dec. 5, 1940): irregular, choppy curve, with undulations varying in frequency; waves of 7-8 per sec. of low voltage (20 mv.); many fast waves throughout curve; hyperventilation increases irregularity and voltage to 50 mv., and fast waves become more conspicuous	Marked impairment for several weeks; difficulty in determining intellectual function because of severe neurotic emotional disturbances

even in those patients who showed psychiatric and electroencephalographic evidence of cerebral dysfunction.

Electroencephalographic Observations.—With the exception of certain patients whose electroencephalograms showed evidences of tension, the preshock electroencephalographic records were normal in the 23 cases studied. After convulsive shock therapy significant disturbances in the cerebral rhythm were noted in 12 patients (2, 4, 5, 7, 9, 10, 11, 15, 16, 19, 22 and 23). These disturbances varied in type and severity. The most severely affected patients (7, 9, 10, 11, 15, 16, 22 and 23) manifested epileptoid disturbances, characterized by 3 and 6 per second waves, spike and wave formations, bicuspid and dicrotic waves and increased amplitude, up to 200 microvolts (see figures). Less severe changes, consisting of increased random or beta activity, were noted in

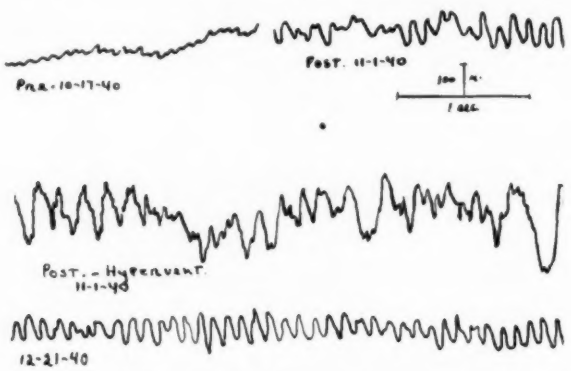

Fig. 1 (case 15).—Pretherapy electroencephalogram, showing alpha waves of low amplitude. Post-therapy electroencephalogram, showing epileptoid curve accentuated by hyperventilation. Electroencephalogram seven weeks after therapy, showing essentially a normal curve except for somewhat increased amplitude of alpha waves.

patients 2 and 19. In patient 4, 18 per second waves occurred (no preshock record was obtained).

In order to study the course of the disturbances in cortical electrical activity, the electroencephalographic tracings were obtained repeatedly on 4 of the most severely affected patients at varying intervals after discharge from the hospital. The observations on these patients will be described in detail, as they indicate that the disturbances in cerebral function (as measured by disturbances in the electroencephalograms) following convulsive shock treatment are largely reversible. Our patients have not been followed long enough at the time of writing to determine whether these cortical disturbances are completely or only partially reversible. In patient 15 (fig. 1) the severe disturbances in cortical

rhythm, consisting of epileptoid, 3 and 6 per second waves of increased amplitude, were completely absent from the electroencephalographic tracing taken one month after discharge and even failed to appear after hyperventilation. The only difference between this tracing and the original preshock tracing, which was taken while the patient was in a profound, almost stuporous, depression, consisted of a change in the amplitude of the alpha waves from a very low voltage to 50 microvolts. It is quite possible that the original low amplitude alpha waves might appear again in a future tracing.[1] Similar changes were observed in patient 10 (fig. 2), in whose electroencephalogram an epileptoid curve with 3 per second waves of 100 microvolts and spike and wave formations developed after the course of metrazol therapy. An electroencephalogram taken six months after discharge revealed a regular alpha

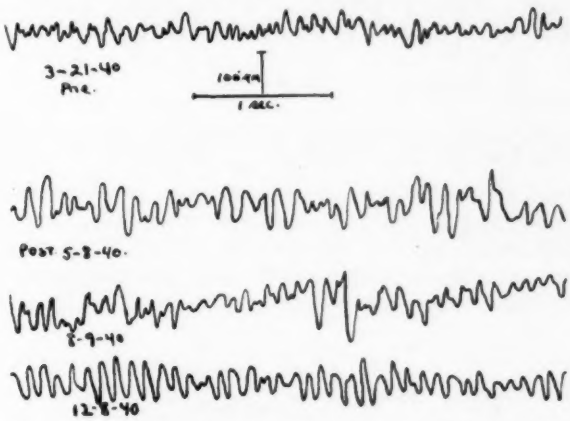

Fig. 2 (case 10).—Pretherapy electroencephalogram, showing normal curve. Post-therapy electroencephalogram, showing epileptoid curve. Three months later the curve is still abnormal. Seven months later it has returned to normal except for occasional 4 per second waves.

rhythm with a maximum amplitude of 100 microvolts. Occasional 4 per second waves were still noted, but the 3 per second waves and the spike and wave formations had disappeared. In this case one finds marked improvement in the cortical rhythm, approaching the normal but still showing evidence of pathologic cortical electrical activity.[2] Patient 22 showed marked improvement in the electroencephalogram two months after discharge, but frankly pathologic waves could be brought out with hyperventilation. In this patient's electroencephalogram severe epileptoid disturbances (fig. 3) developed after only two

1. An electroencephalogram taken six months later still revealed enhanced alpha waves.

2. Six months later the electroencephalogram showed no abnormal waves.

electrically induced convulsions. Six weeks later the curve was fairly regular, with alpha waves of normal voltage, but 3 per second waves appeared during hyperventilation and it took excessively long (twelve and a half seconds) for the curve to return to normal. Reversible

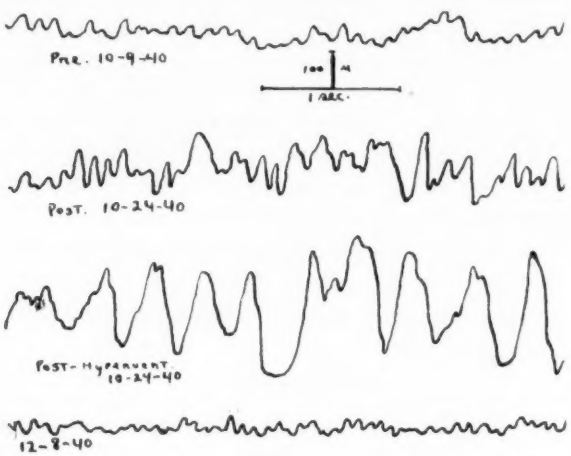

Fig. 3 (case 22).—Pretherapy electroencephalogram, showing normal curve with alpha waves of low amplitude. Post-therapy electroencephalogram, showing epileptoid disturbances, especially on hyperventilation. The electroencephalogram taken six weeks later shows essentially a normal curve, but on hyperventilation (not shown in figure) large 3 and 4 per second waves were still present.

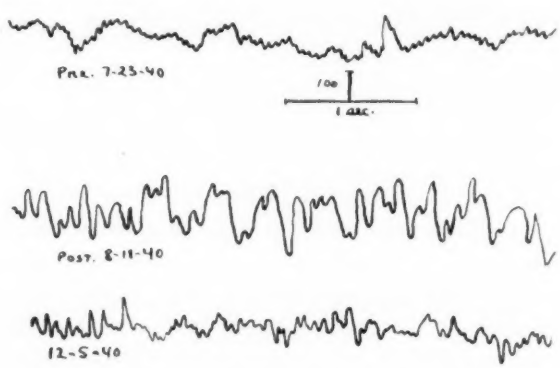

Fig. 4 (case 23).—Pretherapy electroencephalogram, showing absence of alpha waves, marked beta activity and some delta activity. Post-therapy electroencephalogram, showing epileptoid curve. Four months later the electroencephalogram shows improvement, but the curve is irregular and choppy.

changes were similarly noted in patient 23 (fig. 4), in whose electroencephalogram an epileptoid curve developed after nine electrically induced convulsions, characterized by 3 and 6 per second waves, dicrotic

waves, spike and wave formations and increased voltage, up to 200 microvolts. Five months later the curve was irregular and choppy. There were many fast waves, but the 3 and 6 per second waves and the high voltage activity had disappeared and could not be brought on with hyperventilation.[3]

Review of our data to determine the relation between the number of convulsive treatments and the type and severity of the electroencephalographic disturbances does not permit any definite conclusions.

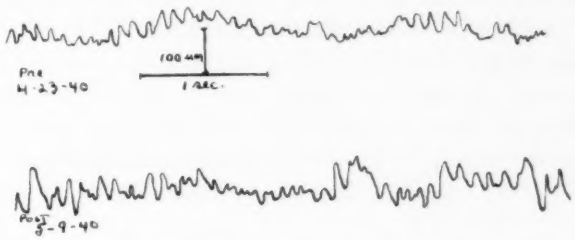

Fig. 5 (case 7).—Pretherapy electroencephalogram, showing good alpha rhythm, with some irregularity. Post-therapy curves showing 6 per second and some 3 per second waves, increased amplitude and suggestion of spike and wave formation.

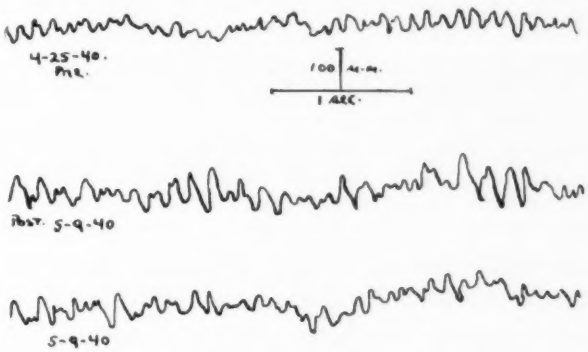

Fig. 6 (case 9).—Pretherapy electroencephalogram, showing fairly normal curve. Post-therapy curve, showing predominantly 6 per second waves of high amplitude, with many notched waves.

Epileptoid dysrythmias occurred after as few as two or three metrazol or electric convulsions (patients 9, 16 and 22). Several patients who experienced ten or eleven seizures failed to show significant electroencephalographic changes. Electroencephalograms were recorded during the course of treatment of only 1 patient. This patient (16) presented an abnormal curve after the third electrically induced convulsion, char-

3. Ten months after treatment the electroencephalogram showed a more regular curve and a much improved alpha rhythm.

acterized by 3 and 6 per second waves, notched waves, questionable spike and wave formations and an increase in voltage. After the completion of the whole course of eight treatments the electroencephalogram became completely irregular; large 3 and 4 per second waves, with amplitudes up to 120 microvolts, and definite spike and wave formations appeared. These observations indicate a direct relation between the number of convulsive seizures and the severity of cortical dysfunction, at least in this case. Confirmatory evidence is found in the fact that intellectual impairment was not present in this patient after the third treatment but was severe after eight treatments. In several patients improvement in the electroencephalogram was encountered after shock treatment, notably in patient 17, whost post-treatment curve showed more regular and more normal alpha waves and less beta activity than the pretreatment curve (fig. 7). The electroencephalogram of patient 12 also showed better alpha waves and less delta activity after eight elec-

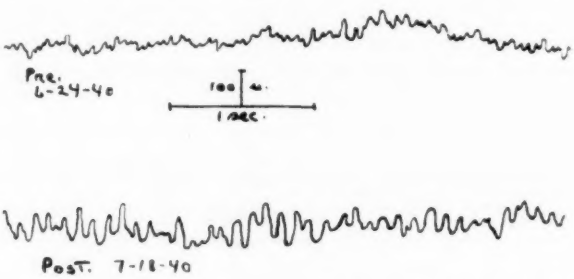

Fig. 7 (case 17).—Pretherapy electroencephalogram, showing few alpha waves, a large quantity of beta waves and much random activity. Post-therapy electroencephalogram, showing a more regular curve and normal alpha waves.

trically induced convulsions. The explanation for these improvements in the electroencephalographic curve may be associated with the decrease in anxiety and tension, which was marked in both of these patients before treatment. Previous studies (Grinker and Serota [4]; Hoagland, Cameron and Rubin [5]) have shown that when anxiety is experimentally induced by appropriate ideational stimuli it may be associated with a marked decrease in alpha activity and an increase in random and rapid activity. Conversely, marked irregularity of the curves and minimal alpha activity are noted in apprehensive, tense subjects at the beginning of the recording. As the subject relaxes in the course of the recording, a more regular curve, with increased alpha activity, develops.

4. Grinker, R. R., and Serota, H.: Studies on Corticohypothalamic Relations in the Cat and Man, J. Neurophysiol. **1**:573, 1938.

5. Hoagland, H.; Cameron, D. E., and Rubin, M. A.: Emotion in Man as Tested by the Delta Index of the Electroencephalogram, J. Gen. Psychol. **19**:227, 1938.

Reports in the neuropsychiatric literature dealing with the changes in electric brain potentials in shock therapy have been limited for the most part to studies of the physiologic disturbances during and immediately after the metrazol convulsion itself. Inasmuch as a number of studies of this kind have been published (Hall, Goodwin and Lloyd [6]; Cook and Walter [7]; Davis and Sulzbach [8]; Strauss and Rahm [9]; Goodwin, Kerr and Lawson,[10] and others), our interest in this paper is confined to the disturbances following the completion of the therapy. Observations similar to ours have been reported by several other observers. Polatin, Strauss and Altman [11] described the electroencephalographic disturbances in 4 cases in which severe disturbances of the sensorium of the "organic" type developed during metrazol convulsive therapy. In these 4 cases the disturbances were tested after the eighth, the sixteenth, the twelfth and the tenth seizure, respectively. Electroencephalograms revealed 3 and 4 per second waves of high amplitude in the first 3 cases and 2 and 3 per second waves in the fourth case. In the course of several weeks both the sensorial and the electrical disturbances returned to normal. An electroencephalographic check-up was made in only 2 cases. These observations differ from ours in that we find abnormal electrical activity in some of our cases as late as five and six months after treatment. The incidence of abnormal brain potentials is ostensibly much greater in our material, but this is obviously due to the fact that Polatin, Strauss and Altman [11] carried out electroencephalographic studies only in those cases in which a severe "organic" type of behavior disturbance was present.

Davis and Sulzbach [8] reported "abnormal fast and slow waves" after metrazol therapy in 4 cases, in 1 of which a porencephalic cyst was present. In 1 case of schizophrenia, thoroughly studied with repeated electroencephalograms, the authors noted changes indicative of damage

6. Hall, E. G.; Goodwin, J. E., and Lloyd, D. P. C.: Physiological Studies in Experimental Insulin and Metrazol Shock, Am. J. Psychiat. **95**:553, 1938.

7. Cook, L. C., and Walter, W. G.: The Electroencephalogram in Convulsion Induced by Cardiazol, J. Neurol. & Psychiat. **1**:180, 1938.

8. Davis, P. A., and Sulzbach, W.: Changes in the Electroencephalogram During Metrazol Therapy, Arch. Neurol. & Psychiat. **43**:341 (Feb.) 1940.

9. Strauss, H., and Rahm, W. E., Jr.: The Effects of Metrazol Injections on Electroencephalograms, Psychiatric Quart. **14**:43, 1940.

10. Goodwin, J. E.; Kerr, W. K., and Lawson, F. L.: Bioelectric Responses in Metrazol and Insulin Shock, Am. J. Psychiat. **96**:1389, 1940.

11. Polatin, P.; Strauss, H., and Altman, L. L.: Transient Organic Mental Reactions During Shock Therapy of the Psychoses: A Clinical Study with Electroencephalographic and Psychological Performance Correlates, Psychiatric Quart. **14**:457, 1940.

to the brain after the eleventh metrazol treatment. These changes became progressively more severe with further treatment, as did the patient's psychosis. One year later the curve was strikingly abnormal, with many 3 per second waves of large amplitude. In this particular case there is little doubt that the metrazol convulsive therapy played an important role in the production of the abnormal electrical activity, but the fact that the electroencephalographic disturbances could be correlated with the patient's disturbed psychotic behavior makes it difficult to evaluate to what extent the electrical disturbances were due to the schizophrenic "process" and to what extent to the metrazol therapy. Another factor to be considered is that the patient received a course of insulin coma treatments after the metrazol therapy. In their report on the consequences of metrazol shock therapy, Read [12] and his co-workers stated briefly that in 13 cases there occurred "interruptions of fast frequency waves of the frontal area by delta waves of high amplitude, [and] characteristic spindles, as seen in grand-mal epilepsy, were present in one patient . . . who suffered spontaneous epileptic attacks after cessation of treatment."

Lemere,[13] in a study limited to schizophrenic patients, demonstrated post-therapeutic depression of alpha activity, followed in two or three days by enhancement of the activity over the preconvulsive pattern, with diminution again in a similar period. Experimental studies of the effect of metrazol convulsions on brain potentials in animals have been limited to the immediate effect. We have encountered few published reports on electroencephalographic studies following a course of induced convulsions. Fleming, Golla and Walter [14] reported that no untoward results followed their use of electric shock therapy and that the electroencephalographic tracings returned to normal. It is evident from the observations on our material that disturbances in brain potentials occur with much greater frequency than the reports on convulsive therapy in the neuropsychiatric literature would indicate and that routine post-therapy electroencephalograms may reveal unsuspected abnormalities even in patients showing little clinical manifestation of cerebral dysfunction.

Effect on Intellectual Functions.—The effect of convulsive shock therapy on the intellectual functions was tested by the customary

12. Read, C. F.: Consequences of Metrazol Shock Therapy, Am. J. Psychiat. **97**:667, 1940.

13. Lemere, F.: Effects on Electroencephalogram of Various Agents Used in Treating Schizophrenia, J. Neurophysiol. **1**:590, 1938.

14. Fleming, G. W. T. H.; Golla, F. L., and Walter, W. G.: Electro-Convulsion Therapy in Schizophrenia, Lancet **2**:1353, 1939.

psychiatric methods for determination of the mental status. These disturbances varied considerably in frequency, severity and duration. They were considered severe when gross impairment of grasp and comprehension, memory, retention and reasoning capacity developed, and moderate when thinking, reasoning and recall were more laborious and slow than the pretherapy mental status and the historical data indicated were normal for the subject. The intellectual function was considered "not impaired" when no disturbances were revealed by these ordinary methods, although it is realized that more detailed psychologic tests might have shown disturbances in finer and more highly integrated intellectual functions.

In the metrazol-treated series (11 patients) 2 (patients 4 and 10) showed severe impairment of the intellectual functions. Both these patients were women, both were depressed and both displayed manic or hypomanic phases during the therapy. They presented a mental status best described as "slap-happy" because of the combination of euphoria and elation and the "organic" type of sensorial defect. In patient 4 the impairment of memory and reasoning following only two metrazol convulsions lasted several weeks, and the "slap-happy" euphoric state, which greatly resembled the type of mental disturbance so frequently observed in patients with tumor of the frontal lobe, was replaced by one of normal affect. This patient's electroencephalogram did not show severe disturbances but contained many 18 per second waves.

In patient 10, after five metrazol convulsions, more severe intellectual disturbance developed and persisted for many weeks after the postdepression manic phase had subsided. Reexamination six months later, after the patient had been adjusting successfully in her social life and in her work as a saleswoman for several months, indicated that slight impairment was still present. The electroencephalogram, which showed severe epileptoid disturbances after the metrazol treatment, at the time of reexamination, six months later, revealed striking improvement in the character of the curve, with return to a normal alpha rhythm. Certain abnormalities, such as occasional 4 per second waves and increased amplitude (100 microvolts), were still present.

Impairment in intellectual functions occurred much more frequently in the electrically treated patients, that is, in 8 out of 13 (patients 12, 15, 16, 17, 19, 21, 22 and 23). In most of these patients the impairment lasted one to several weeks. Mild changes were still present in 1 patient after several months, although the patient, a woman of 31, apparently was making a satisfactory adjustment in her work as a law secretary. These mental disturbances were of the same type as those observed after metrazol, of the so-called organic type, often accom-

panied by a euphoric, "slap-happy" state, in which the higher intellectual faculties were conspicuously affected. As in the metrazol-treated patients, impairment of intellectual function occurred after as few as two electrically induced convulsions (patient 22), but the most marked disturbances occurred in patients who experienced more (patient 8, after eight treatments; patient 15, after five treatments; patient 16, after eight treatments; patient 19, after eleven treatments; patient 21, after eight treatments, and patient 23, after nine treatments). The intellectual disturbances in these patients became increasingly conspicuous during the latter part of the course of treatments. These observations suggest that the degree of cerebral dysfunction varies directly with the number of convulsive treatments. This is in agreement with the experience of others (Ziskind[15]). Kalinowsky and Barrera,[16] on the other hand, failed to observe "mental sequelae" in their electrically treated patients. In most instances the electroencephalographic abnormalities and the changes in the sensorium were mutually confirmatory of impaired cerebral function, but in several patients electrical dysrythmias were observed without apparent disturbance in intellectual functioning, and, vice versa, severe intellectual disturbances developed in patients who did not show significant electroencephalographic abnormalities (patients 7, 12, 17 and 21). In 1 instance (patient 17) the postshock electroencephalographic curve was more regular and contained more alpha and less beta activity than the preshock curve, despite the fact that considerable intellectual impairment and the typical "slap-happy" manic phase developed.

COMMENT

From the neuropsychiatric and the electroencephalographic studies of our material it is evident that in a certain proportion of patients metrazol-induced and electrically induced convulsions used in the customary therapeutic doses may produce definite disturbances in cerebral functions. As determined by changes in the electroencephalograms, these disturbances occurred in approximately 50 per cent of patients. A somewhat smaller number (10 out of 23) revealed cerebral disturbances as determined by changes in intellectual functions, but this proportion would probably have been higher if more accurate psychologic methods of examination had been employed (later comfirmed by Rorschach studies). These disturbances in brain function may last weeks or months. Our longest period of observation showed that slight

15. Ziskind, E.: Memory Defects During Metrazol Therapy, Arch. Neurol. & Psychiat. **45**:223 (Feb.) 1941.

16. Kalinowsky, L., and Barrera, S. E.: Electric Convulsion Therapy in Mental Disorders, Psychiatric Quart. **14**:719, 1940.

disturbances were still present after six months. Obviously, a longer period of observation is required before any definite conclusions can be drawn, but the evidence from our data indicates that the damage to the brain cells, whatever its character may be, is for the most part reversible.

It is worthy of note that none of the 23 patients showed any clinical sign of a convulsive disorder, although the electroencephalographic tracings frequently showed disturbances closely resembling those seen in cases of clinical epilepsy. Long term observation with this possibility, as well as other organic neuropsychiatric disorders, in mind is obviously necessary. A single, poorly documented, questionable case of convulsive disorder manifesting itself some months after a course of metrazol therapy was reported by Hartenberg.[17] Read[12] and his co-workers also made a brief allusion to a patient who had "spontaneous epileptic attacks after cessation of treatment." We can add 1 case of our own, not included in the series on which this report is based, in which the patient had two generalized epileptiform convulsions several weeks after receiving two electrically induced convulsive treatments for a neurotic depression. These convulsions occurred one week after severe rectal hemorrhages due to a rectal polyp had resulted in severe hemorrhagic anemia. No history of epilepsy or evidence of disease of the brain was present. The post-therapy electroencephalogram had shown some disappearance of alpha waves and moderate delta activity but no 3 or 4 per second waves or other cerebral dysrythmia suggestive of an epileptoid disturbance. Nevertheless, it is conceivable that some damage to the cortical neurons was produced, that the convulsive threshold was lowered and that after a severe rectal hemorrhage anemic circulatory disturbances in the brain produced added functional disturbances in the cortical neurons, resulting in the convulsive seizures. These observations suggest that a convulsive disorder may develop in rare instances as a result of convulsive shock therapy.

That actual structural damage to the central nervous system may result from convulsive therapy is indicated in various reports published in recent years. Strecker, Alpers, Flaherty and Hughes[18] reported neuropathologic studies on brains of monkeys after series of metrazol convulsions. In 4 out of 7 animals they observed cellular changes and subarachnoid hemorrhages. These animals received totals of from thirty to one hundred and forty-seven minutes of convulsions, a factor of

17. Hartenberg, M.: Epilepsie consécutive à un traitement par le cardiazol, Ann. méd.-psychol. (pt. 1) **98**:73, 1940.

18. Strecker, E. A.; Alpers, B. J.; Flaherty, J. A., and Hughes, J.: Experimental and Clinical Study of Effects of Metrazol Convulsions, Arch. Neurol. & Psychiat. **41**:996 (May) 1939.

some importance in the production of the pathologic changes, in the opinion of the authors. Weil and Liebert [19] described the histologic changes in the brains of 6 psychotic patients who had been treated with metrazol convulsions. The outstanding histopathologic feature was marked hypertrophy and hyperplasia of astrocytes and, to a lesser degree, of microgliocytes. They stated that these changes were strikingly similar to their earlier observations on the brains of rabbits after experimental metrazol injections. Finley and Brenner [20] also noted mild proliferation of astrocytes in the brains of monkeys after a series of metrazol convulsions. In addition, small foci from which cortical nerve cells had disappeared were seen. Neurohistologic changes in mice following metrazol convulsions were also reported by Cleckley, Bowles and Mettler.[21] Demineralization of ganglion cells in the brains of rabbits was observed by Liebert and Heilbrunn [22] after large amounts of metrazol. On the other hand, Winkelman and Moore [23] found relative absence of involvement of the central nervous system in cats after metrazol convulsions. Except for pyknosis of scattered cells of a minimal degree, the cell pictures were described as comparing favorably with those of control animals, and no striking glial reaction was noted. The majority of the reports, however (see Cleckley and associates [21] for more complete review of the literature), indicated that pathologic alterations do result after metrazol-induced convulsive seizures.

At the time of this writing electric shock therapy has been in use in this country for only a short period, so that few pathologic studies have as yet appeared in the literature. Anatomic studies on animals by Cerletti and Bini,[24] to whom is owed the original use of electroshock therapy, revealed only reversible changes in the brain. A timely report by Heilbrunn and Liebert,[25] who examined histologically biopsy speci-

19. Weil, A., and Liebert, E.: A Neuropathologic Study of Six Cases of Psychoses Treated with Metrazol, Tr. Am. Neurol. A. **66**:162, 1940.

20. Finley, K. H., and Brenner, C.: The Neuropathology in Monkeys Resulting from a Series of Metrazol Convulsions and Insulin Comas, Tr. Am. Neurol. A. **66**:181, 1940.

21. Cleckley, H.; Bowles, L., and Mettler, F. A.: Histologic Changes Following Metrazol Convulsions, Arch. Neurol. & Psychiat. **43**:948 (May) 1940

22. Liebert, E., and Heilbrunn, G.: Mineral Content of the Brain: Changes in Experimental Animals Following Injections of Insulin and Metrazol, Arch. Neurol. & Psychiat. **43**:463 (March) 1940.

23. Winkelman, N. W., and Moore, M. T.: Neurohistopathologic Changes with Metrazol and Insulin Shock Therapy, Arch. Neurol. & Psychiat. **43**:1108 (June) 1940.

24. Cerletti, U., and Bini, L.: L'elettroschock, Arch. gen. di neurol., psichiat. e psichoanal. **19**:266, 1938.

25. Heilbrunn, G., and Liebert, E.: Biopsy Studies of the Brain Following Artificially Produced Convulsions, Arch. Neurol. & Psychiat. **46**:548 (Sept.) 1941.

mens of the brain obtained from rabbits at varying intervals after single metrazol and electric convulsive seizures, revealed definite pathologic alterations in nerve cells. These workers expressed the opinion that these disturbances were largely, but not completely, reversible after one hour. Our data fail to shed any light on the character of the damage to the brain, but its reversible nature is suggested by the return to normal, or approximately normal, function or the marked improvement of cerebral function. Further observation on our patients is necessary before definite conclusions can be drawn regarding the possibly permanent or wholly reversible nature of these disturbances. Our data do not indicate that any particular region of the cortex is affected by the convulsive treatments, but the electroencephalographic studies were not carried out with a localizing technic. The impairment of the sensorium is not indicative of any focal localization of the pathologic process, inasmuch as the intellectual functions are a function of the cortex as an integrated whole and may be severely disturbed by diffuse cortical processes. As already stated, no positive neurologic changes indicative of gross disturbances in the brain were found.

It is of interest to analyze our material as to the comparative effects on cerebral function of metrazol and electric shock therapy. The two groups are comparable in the number and type of patients and in the varying numbers of convulsions experienced. In the series of 11 metrazol-treated patients, 7 showed electroencephalographic evidences of cerebral disturbance, only 2 of whom displayed conspicuous impairment in intellectual function. Of these 2 patients, patient 4 showed 18 per second waves, but the other (patient 10) showed severe electroencephalographic changes of epileptoid type. In the electric shock series of 12 patients, electroencephalographic and psychologic (impaired sensorium) evidence of cerebral dysfunction developed in 5, while 3 additional patients showed psychologic impairment without electroencephalographic abnormalities, thus making a total of 8 patients in whom one or both manifestations of cerebral dysfunction were present. One of these patients (12) had severe disturbances of the sensorium, but the electroencephalographic curve contained better alpha and fewer delta waves than the preshock record. Thus, the number of patients in whom signs of cerebral dysfunction were found was approximately the same in the metrazol and in the electric shock series, 7 and 8, respectively, or a total of 15. Qualitatively, however, more instances of severe disturbances were encountered in the electrically treated patients, and epileptoid disturbances of the brain waves occurred more frequently in the electric shock series.

The investigation and interpretation of brain action potentials in persons with normal and with disturbed cerebral function are still in their early stages, so that caution must be exercised before one considers certain deviations to be indicative of cerebral damage. Disturbances in cerebral function, however, which manifest themselves as impaired intellectual functioning, are unquestionably indicative of a disordered cortical activity. In consideration of both the greater incidence of impaired intellectual functioning encountered in the electrically treated patients than in the metrazol-treated patients and the greater incidence of epileptoid disturbances in the action potentials, the conclusion that electric shock produces more severe damage to the brain than metrazol shock seems justified.

Attempts to correlate the post-therapy damage to the brain with other factors have not been successful. Changes were found in both male and female patients, but the number is too small to permit any statistical evaluation.

Similarly, no correlation is present between the age and the reaction to treatment. Cerebral damage occurred in the young as well as in the middle-aged adults. In fact, patients 22 and 16, aged 31 and 34, respectively, presented as severe evidences of damage to the brain as patients 10, 15 and 23, aged 51, 49 and 57, respectively.

The duration of the illness seems to bear no relation to the effect of therapy on cerebral function, as evidences of damage to the brain were noted in patients whose illness had been present weeks, months or several years.

The incidence of damage to the brain could not be correlated with any particular type of psychiatric condition. No patients with lesions of the brain, as far as could be determined by ordinary neuropsychiatric examination, were included in this series. All patients, with the exception of 1 with schizophrenia, had affective disorders, either primary or secondary, such as the neurotic depressions and the depressive mood reactions in schizophrenic or paranoid states. The number of cases in each diagnostic group is too small to be of statistical value in this regard.

A detailed theoretic discussion of the possible mechanism by which convulsive shock therapy produces such spectacular changes in patients with affective disorders is not within the scope of this communication (Grinker and McLean [26]). Suffice it that our observations fail to clarify this extremely controversial and obscure problem. Similarly, our experience with psychotherapy of various types in conjunction with convulsive shock therapy, although no formal study of our material as a whole has been carried out, fails to contribute to our understanding of the mechan-

26. Grinker, R. R., and McLean, H.: The Course of a Depression Treated with Psychotherapy and Metrazol, Psychosom. Med. **2**:119, 1940.

ism of recovery in this type of therapy. Some patients improved with little or no direct or intensive psychotherapy and remained well, while in the cases of others we consider that the intensive psychotherapy played a considerable part in the process of recovery. The subject of psychotherapy in conjunction with shock therapy in cases of depression is a fascinating one, especially for the analytically oriented psychotherapeutist. We have had a number of cases in which modified short analytically oriented therapy (as exemplified by the report of Grinker and McLean) and, in 1 case, classic analysis (N. A. L.) were made possible by the breaking up of the depressive inhibition of thinking and speaking by means of convulsive therapy. Certain of these psychologic and psychotherapeutic observations will be made the subject of a future communication.

CONCLUSIONS

A series of 23 patients with affective reactions treated with metrazol-induced and electrically induced convulsions were studied clinically and electroencephalographically to determine the presence and extent of post-therapeutic disturbances in cerebral function.

Of 23 patients, 14 recovered or improved and 9 did not improve. Early recurrences were included in the category of no improvement. In contrast to previous forms of treatment, the striking feature was the spectacular rapidity of recovery of the patients who were cured.

Evidence of disturbed cerebral function was present in 50 per cent of the patients as indicated by changes in the electroencephalogram and in 45 per cent of the patients as shown by changes in intellectual function.

In the most severely affected patients epileptoid disturbances in the electroencephalogram developed, consisting of 3 per second waves, bicuspid and dicrotic waves, spike and wave formations and greatly increased amplitude. The post-therapeutic clinical evidences of impaired cerebral function consisted of an "organic" type of sensorial and intellectual impairment.

Recovery from these disturbances of cerebral function occurred in most patients in a few weeks. In the more severely affected patients evidences of impaired cerebral function sometimes lasted as long as six months.

Recovery or improvement is apparently not dependent on the presence of such changes in cerebral function as are shown by our methods of electroencephalographic examination and tests for mental status.

DISCUSSION

DR. KNOX H. FINLEY, Boston: Dr. Lesko and I have had occasion to take electroencephalograms before and after metrazol treatment on 9 patients, and our findings agree with those reported by Drs. Grinker, Levy and Serota. We found,

also, that in general the greater the number of treatments the more likely one was to find temporary or permanent changes in the electroencephalogram. In general, our experience in this small series was that in patients receiving six or less injections, most of which were followed by convulsions, changes lasting as long as a few days or weeks were not likely to occur. The patients receiving in the neighborhood of ten treatments were likely to show temporary changes lasting days or weeks, while the 2 patients who received nineteen or twenty injections, respectively, showed permanent changes in their electroencephalograms. By permanent I mean changes persisting over a year and a half. I should add that from the 2 patients in whom we found permanent changes we were unable to obtain records before the series of treatments was started, but these were the only ones in the series of 9 patients in whom permanent neurologic signs developed as a result of the shock treatment.

Dr. Marjorie Meehan, Princeton, N. J.: Was there any correlation between the symptoms and the electroencephalographic changes? In other words, did these patients, when their electroencephalographic patterns returned to normal, show any recurrence of symptoms? The effect of the convulsions is not understood. Perhaps the change in the electroencephalogram represents some factor which has therapeutic value.

Dr. Herman Selinsky, New York: Has Dr. Levy any impression as to the difference in electroencephalographic abnormalities provoked by the metrazol convulsion and by the electric shock? Does one produce a more intense reaction than the others?

Dr. Roy R. Grinker, Chicago: This mechanistic approach to psychiatry is being used extensively at present; I think it can be stated unequivocally that it is fraught with extreme danger. There is not only an emotional but an intellectual change in the patients. Those who have seen fighters that have been in many battles know the "punch-drunk" or "slap-happy" conditions and may recognize a similar state in some patients after shock therapy. This does not last long, at least in its striking form. However, careful studies by means of a battery of psychologic tests reveal a definite "organic" change in memory which does not entirely clear up.

Electroencephalographic abnormalities which are reminiscent of certain forms of epilepsy sometimes clear up entirely. Often the so-called normal alpha rhythm increases greatly in voltage, making one suspicious that irreparable damage to the brain has been produced.

Dr. Leibert, of Elgin, Ill., reported that 8 patients receiving metrazol treatment had recurrent epileptic attacks which could be classified as epileptic and had to be treated with anticonvulsants. There may be a place in psychiatry for this type of therapy. Its indications may be exactly delimited in the future, but I present these facts now to indicate that there is grave danger in using such procedures as metrazol and electric shock in treatment of human beings.

Dr. Harry C. Solomon, Boston: I take it no one wants to continue the debate that Dr. Grinker has started on the validity of using this type of treatment of the psychoses. Perhaps it is just as well at this point that we do not do so.

Dr. Norman A. Levy, Chicago: In answer to Dr. Finley's remarks, we did find severe changes in patients who received less than six treatments.

I presented 1 patient, a young woman, who received only two treatments. We have others who received three treatments and also showed severe changes.

DR. KNOX H. FINLEY, Boston: How long did these changes last?

DR. NORMAN A. LEVY, Chicago: They subsided over a period of several months after the cessation of the treatments. We found no correlation between the symptoms and the improvement in the electroencephalogram; there were no recurrences with such improvement.

In answer to Dr. Selinsky, we found that quantitatively there does not seem to be much difference between the electrically induced and the metrazol-induced series, as to the number of patients who showed disturbances, but qualitatively we found that the electrically induced convulsions produced more severe disturbances in the electroencephalogram and in the intellectual functions of the patients.

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SPECIAL ARTICLE

CLINICAL NOTES FROM A TRIP TO GREAT BRITAIN

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The face of British medicine has greatly altered, but the medical profession as a whole has never been more active. Harley Street is empty and the consultants are widely scattered. Yet in spite of the scars which were left after the battle of Britain, life in London goes on calmly and in its normal channels, for the most part. The administrative center for medical affairs is here, including the headquarters of the Medical Services, the Ministry of Health and the Medical Research Council. The Royal Society and the Royal Society of Medicine are active in various ways. The Royal College of Surgeons, although its priceless Hunterian collection is gone, carries on vigorously. All this illustrates the practical futility of indiscriminate bombing.

In the reorganization of British medicine the Emergency Medical Service (E. M. S.) has played the most important role. The details of this organization may be discussed, for they are printed in their own pamphlets. The general plan was worked out by the Ministry of Health, which retains directing control. Except for the special hospitals under the army, navy and air force, which are relatively few, all the best hospitals in Great Britain have been enrolled in the Emergency Medical Service. They are included in a comprehensive scheme to serve the displaced population of Great Britain and are organized for rapid evacuation of patients from any areas in which fighting may occur. These hospitals admit immediately and at the expense of the government all civil and military casualties that may result from enemy action. They also admit ordinary patients on a different basis. A large number of centers have been set up for the various medical specialties, and E. M. S. consultants go about through the country wherever needed.

In this great organization special centers for the medical specialties are set up and specialist consultants appointed, one for each of the major subdivisions. The principal specialties from the point of view of the number of centers are, in order, orthopedics, neurosurgery, thoracic surgery, treatment of neurosis and plastic surgery.

The plan for evacuation of casualties and the sick from London is somewhat as follows: Each of the large London hospitals has become

the focal point of a sector which extends out from the center of London for a distance of 40 to 50 miles (64 to 80 kilometers). There are nine such sectors, for London Hospital, St. Bartholomew's Hospital, University College Hospital, Middlesex Hospital, St. Mary's Hospital, St. George's with Charing Cross Hospital, St. Thomas's Hospital, King's College Hospital and Guy's Hospital respectively. Each of these sectors is shaped somewhat like a piece of pie, with the point in London. The medical and nursing staff in the various Emergency Medical Service hospitals in each sector is provided, to some extent, from the corresponding London hospital. Patients seen in the outpatient clinics of the parent hospital are sent out into the corresponding sector, and the bomb casualties which may be brought to each London hospital are likewise sent out rapidly by ambulance in the corresponding sector after initial operation or first aid treatment. Thus the teaching hospitals are being used for the treatment of emergency patients, to conduct outpatient clinics and to serve as evacuation centers.

The teaching of medical students is being carried on by each of the London hospital medical schools under the new conditions of suburban medicine. Some of the more wealthy hospitals have housed their students together; others have allowed them to be billeted where they can find accommodation. All medical students are exempted from military service, even in the first year.

Research on secret practical problems in Britain is well organized, well directed, sometimes brilliant. Control and initiative in such matters has been taken over by the Medical Research Council, under the leadership of Sir Edward Mellanby. Numerous special committees have been set up in close cooperation with representatives of the army and air force to study specific problems, and these committees are driving ahead with the help of individual workers in selected laboratories to whom work is delegated.

Neurosurgery in Great Britain has altered somewhat from that in time of peace as far as clinical material goes. It has altered very much in its organization.

There is an increase in the number of head injuries. This is due to the use of the motorcycle in the hands of dispatch riders. The blackout and the movement of troops on maneuvers bring a regular quota of road accidents. The use of crash helmets, modified football helmets, has reduced the mortality from motorcycle crashes. The survivors usually have fractures of the lower extremities, especially the femurs.

As the result of bomb explosions, there are many who die immediately of head injury. On the other hand, among those who are thus injured and not killed, the percentage of head injuries is not very high. This

was pointed out by Zuckerman,[1] who found on examining those killed by such explosions that the great majority had severe head injuries. Such injuries were due to flying stones or metal, not to the impact of the blast itself.

Zuckerman concluded that only about 1 per cent are actually killed by true blast. Blast consists in a wave of positive pressure which passes rapidly outward from the point of explosion and is followed by a succeeding wave of negative pressure. This, in turn, is followed by a strong wind. These phenomena produce violent and unpredictable displacement of nearby objects. Aside from displacement, the principal effect of blast on man or beast is to cause bleeding in the lung, and when death does occur it seems to be pulmonary.

Consequently, those nonfatal head injuries which result from bomb explosion resemble the head injuries of civil practice except that they are more apt to be complicated and the paranasal sinuses depressed. They are very dirty; dust and gravel may be ground into the skin. This is true of such injuries in general. There may be face burns because, so often, the contents of a fireplace are blown out into the faces of those who sit in cozy fashion about it; eyes may be put out or bits of glass driven into soft tissues.

The modern aerial bomb has an enormous bursting charge. Small fragments, such as bits of its casing, may fly off at such a high rate of speed that they penetrate to a considerable depth, and unsuspected minute fragments have been discovered only by roentgenographic examination to be lodged within the brain or other parts of the body. These fragments are probably rendered sterile by heat. At all events they may usually be left alone.

The use of sulfanilamide and its derivatives, both locally and by oral administration, has very considerably lengthened the time after injury that one may carry out excision and closure. Sulfanilamide, sulfadiazine (2-[paraaminobenzenesulfonamido]-pyrimidine) and sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) can all be used on the brain itself before closure, without increasing the severity of scarring (Russell and Falconer[2]; Hurteau[3]; Botterell, Carmichael and Cone[4]).

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1. Zuckerman, S.: Experimental Study of Blast Injuries to Lungs, Lancet **2**:219 (Aug. 24) 1940.

2. Russell, D. S., and Falconer, M. A.: Local Effects of Sulphonamides on Rabbit's Brain, Lancet **2**:100-101 (July 27) 1940.

3. Hurteau, E. F.: The Intracranial Use of Sulphonamides: Experimental Study of the Histology and Rate of Absorption, Canad. M. A. J. **44**:352-355 (April) 1941.

4. Botterell, E. H.; Carmichael, E. A., and Cone, W. V.: Sulphanilamide and Sulphapyridine in Experimental Cerebral Wounds, J. Neurol. & Psychopath. **4**:163-174 (July-Oct.) 1941.

Certain of the neurosurgeons, such as Geoffrey Jefferson of Manchester, have taken to placing sulfathiazole routinely within all craniotomy incisions before closure.

It is unwise for me to discuss here specific military plans and arrangements as they may have been worked out in Great Britain. I may, however, express a personal opinion as to what is the ideal arrangement for the neurosurgery of an army in action in this war. It has to be granted, first of all, that rapid movement and many casualties, in a short space of time, will interrupt long periods of waiting and preparation.

The maximum flexibility of organization is therefore essential. The choice would seem to be between mobile units as against fixed base centers, with adequate facilities for transportation to such centers. Either the army must be followed closely or the wounded must be collected and transported with speed to a great distance.

Mobile head units, fully provided with portable equipment and other specialized units, have been developed. But, except in unusual circumstances, they can hardly cope with the conditions of modern warfare, for if such teams are close to the fighting the wounded cannot be sorted out adequately. It is probably true, however, that under special circumstances such a mobile unit might do excellent work, especially when attached to a larger general base hospital or a field ambulance.

But the more effective organization is as follows: Establish a neurologic and neurosurgical base hospital to which cases can be referred during the long periods of relative inactivity. During times of great activity some of the neurosurgeons must be moved out, wherever needed, to those large general units nearest the fighting. They should work there until after the deluge of fresh wounds has ceased. After that, these neurosurgeons on loan should return to the neurosurgical center just as soon as decreased activity makes triage (the sorting of wounded) possible.

A military power which has control of the air can transfer patients by air ambulance, and actually an adequately organized air ambulance is the only really effective way of meeting the problems of care of the sick in modern warfare.[5] An air ambulance which has small collecting planes that can land and take off in small space and large, fast transport planes, could conduct proper triage and could sort out the patients for separate hospitals. In that case the neurosurgical personnel could be kept together and thus receive and handle properly cases of head and spine injury, with a great saving of life.

5. It is an unwelcome commentary on the capacity of the democracies to prepare for war that only Germany has, so far, developed an air ambulance service, except on paper.

In the vicinity of an army a neurologic hospital should be staffed with able specialists in such a way as to be a neurologic and neurosurgical center. This has been done by the British and by the Canadians. In times of inactivity neurosurgery is relatively slack and neurology active, with cases of psychoneurosis, headache and other neurologic conditions. In active periods the reverse will be true. During the slack times consultants may be drawn from the neurologic center for use far and wide. But it is quite impossible to staff permanently all the general hospitals with responsible, fully trained neurologists and neurosurgeons, for the amount of material is too small proportionally during the long periods of inactivity.

In closing, I should like to make some reference to the general problem of psychoneurosis in Great Britain, particularly as misleading reports have appeared in the press. I had every opportunity to study this problem first hand and took occasion to discuss the matter with Dr. Gordon Holmes, neurological consultant to the Emergency Medical Service; Dr. Aubrey Lewis, psychiatric consultant to the Emergency Medical Service; Colonel Rees, psychiatric consultant to the director general of the Royal Army Medical Service, and others.

Not only is there no increase in psychoneuroses in the civil population, but there is an actual decrease as compared with peace time. This is an established fact. It is part of the general national reaction of quiet defiance that is immediately apparent, and thrilling, to a new arrival in Britain now. It is evidence, also, that the war insurance scheme is working well and that the mobilization of man power and woman power, which has progressed very far indeed, has not introduced unwise aspects of compulsion.

It might be urged that badly shocked persons had withdrawn from London and other bombed areas to "lick their wounds." But this is not the correct explanation, inasmuch as 2,000 beds set aside by the Emergency Military Service for use either by military personnel or by civilians had practically no civilian occupancy. In a census of five large Emergency Military Service hospitals open to civil and military cases, in December 1940 there were 600 military and 3 civilian cases. In the same hospitals in January 1941 there were no civilian cases and in February 550 military and 4 civil cases.

Civilians who have been injured by enemy action are handled under Emergency Military Service regulations as follows: They are allowed three weeks only without diagnosis. Then the patient, if his condition is classed as "functional" or "undiagnosed," must choose between hospital study and return to work. The choice is usually for the latter.

On the other hand, the soldier can "get back to his own work" only by entering the hospital. So the "wish factor" is important. For most

men in the army this war has, so far, hardly been a war at all. Owing to inactivity and personal distaste for military routine there has been about as much psychoneurosis and malingering as would be expected.

On the other hand, when one comes to consider more carefully the military patients who were actually admitted to hospitals labeled as cases of psychoneurosis, it becomes apparent that in spite of the comparatively large number, those with true psychoneurosis are few. The condition of the great majority deserves some other name.

Many of these men find themselves in the hospital because it is the only way of getting them out of a unit where they are not proving satisfactory. It is said that in the old days the best soldier proved to be the country bumpkin. He could not think and was not called on to do so. Now, the men have to think to be useful. If they prove useless, the commanding officer can get rid of them only on medical grounds; so the mentally inadequate are eliminated with the help of the medical officer, who can do so only by admitting them to the hospital as psychoneurotic.

Patients of this type seem to be well handled, in general, by common sense methods and without resort to the complicated technics of psychoanalysis. In neurosis centers a point is made of studying a soldier's aptitudes and he is often changed from one branch of the army to another; for example, a man who is unhappy in the paymaster's department may do well driving a lorry.

A frequent source of trouble is worry on the part of a soldier or sailor about the condition of his own family, particularly if they live in an area exposed to bombing. This difficulty is improved by the practice of granting leave to return home every three months when this is possible.

In the Canadian army similar difficulties present themselves. Because of the great distance they are apt to be worried about their families far away, and this may well apply to American forces as well. A letter may have come to say that a soldier's wife is in financial difficulties or is neglecting the children or is interested, let us say, in a sailor. It is not possible to send the man home on leave, and here develops a real difficulty that calls for an adequate social service system capable of investigating conditions in the homes of those soldiers who have reason for anxiety. It calls, also, for a means of rapid communication from and to the men on active service.

As Colin Russel has pointed out, there is a modern change in the style of neurotic patterns. Whereas in the last war the soldier who could not "stand the gaff" considered himself a victim of "shell shock" and might well show hysterical phenomena, paralyses or anesthesias, in this war he has learned that the complaint of headache following a

blow on the head is apt to serve as entitlement to invalidism and discharge. He finds the medical officers willing to label him as a sufferer from "post-traumatic head syndrome," a term quite as unsatisfactory as shell shock.

It is therefore of the greatest importance that medical officers should realize that, rather than use such vague terms, it is preferable to make a specific diagnosis even if it involves a small risk of error. A strong line in regard to these cases will make an outlet from the cul-de-sac in which they are otherwise placed. Post-traumatic meningeal headache is a curable condition; fatigue headache is curable; headaches due to eye-strain are curable; anxiety states are curable; the circulatory instability which may follow injury is associated with headache, and it also is curable. The remaining complainers should be recognized in their true colors. For some of them the virtue of service in a labor battalion should not be overlooked.

From the Department of Neurology and Neurosurgery, McGill University, and the Montreal Neurological Institute.

3801 University Street.

News and Comment

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY, INC.

At a meeting of the American Board of Psychiatry and Neurology, Inc., held on May 16, 1942, the following diplomates were certified:

Neurology.—By Examination: *Harvey Bartle Jr., Philadelphia; Charles Brenner, Boston; Robert Lawrence Craig, Durham, N. C.; Arthur D. Ecker, Syracuse, N. Y.; Saul I. Heller, New York; Charles M. Jessico, Duluth, Minn.; Paul Michael Levin, Dallas, Texas; Charles I. Oller, Philadelphia; Stephen W. Ranson, Fort Custer, Mich.; *Earl Saxe, Fort Dix, N. J.; *Louis Bernard Shapiro, Elgin, Ill.; *Israel Ronald Sonenthal, Chicago; David Wies, Waverley, Mass.

Neurology.—On Record: Arthur Weil, Chicago.

Psychiatry.—By Examination: George Harold Alexander, Providence, R. I.; Benjamin Apfelberg, Forest Hills, N. Y.; Jesse O. Arnold II, Worcester, Mass.; Nita Mieth Arnold, Chicago; Janet Stetson Barnes, East Gardner, Mass.; G. Burnham Beaman Jr., Boston; Rex Blankinship, Richmond, Va.; Frank Scannell Broggi, Framingham, Mass.; Louis Samuel Chase, Boston; Richard C. Cooke, Waltham, Mass.; Albert Loyal Crane, Evansville, Ind.; Leolia Agnes Dalrymple, Boston; Franklin Smith DuBois, New Canaan, Conn.; H. Carter Dunstone, Ypsilanti, Mich.; Norris Butler Flanagan, Boston; Samuel Friedman, Newtown, Conn.; Samuel Futterman, New York; Israel P. Glauber, New York; Leon Nathaniel Goldensohn, New York; Frank Abram Hale, New York; Volta Ross Hall Jr., Arlington Heights, Mass.; Francis J. Hamilton, New York; Francis T. Harrington, Dallas, Texas; Gerhard B. Haugen, Baltimore; Henry Lee Hartman, Taunton, Mass.; Emeline P. Hayward, New York; Marcel Heiman, Mount Pleasant, Iowa; L. Clovis Hirning, Valhalla, N. Y.; Paul Hletko, Manteno, Ill.; Paul Holmer, Reading, Pa.; Reynold A. Jensen, Minneapolis; S. Harvard Kaufman, Philadelphia; William H. Kelly, Lansing, Mich.; Ralph F. Kernkamp, Eloise, Mich.; Harry L. Kozol, Boston; Louis S. Lipschutz, Eloise, Mich.; Henry G. Lonsdale, Elgin, Ill.; Harold L. Mitchell, Pittsburgh; Jane E. Oltman, Newtown, Conn.; George E. Peatick, Philadelphia; Gerhart J. Piers, Elgin, Ill.; I. Paley Rak, Boston; John F. Regan, Howard, R. I.; Joseph Franklin Robinson, Wilkes-Barre, Pa.; *Augustus S. Rose, Boston; Albert A. Rosner, New York; *Alexander T. Ross, Fort Benjamin Harrison, Ind.; Nathaniel Ross, New York; Samuel H. Ruskin, Eloise, Mich.; John A. Russell, Washington, D. C.; *Hawley S. Sanford, Detroit; H. A. Sears, Kalamazoo, Mich.; Abraham Simon, Kankakee, Ill.; Leo Angelo Spiegel, New York; Robert J. Stein, Lincoln, Neb.; Saul Steinberg, Norristown, Pa.; *Milton N. Tarlau, Forest Hills, New York; John Butler Tompkins, Waverley, Mass.; Jewitt I. Varney, White Plains, N. Y.; George Leland Wadsworth, Howard, R. I.; Marianne Wallenberg, Manteno, Ill.; Jack Weinberg, Chicago; Charles Edwin White, Howard, R. I.; Samuel Wick, Wauwatosa, Wis.; Meyer A. Zeligs, Bethesda, Md.

Psychiatry.—On Record: Meade Stith Brent, Petersburg, Va.; Felix Deutsch, Boston; Helene Deutsch, Cambridge, Mass.; Emil Zola Levitin, Peoria, Ill.;

*Denotes complementary certification.

Harry Barney Levey, Chicago; Benzion Liber, New York; William Kerr McCandliss, Trenton, N. J.; George K. Pratt, Westport, Conn.; Edward Gould Rowland, Trenton, N. J.; Rene Arpad Spitz, New York; Walter H. Squires, Eloise, Mich.

Neurology and Psychiatry.—By Examination: Raymond DeLacy Adams, Boston; Richmond James Beck, Huntington, L. I., N. Y.; Robert William David, Denver; George Frumkes, New York; Roy R. Grinker, Chicago; Samuel Bernard Hadden, Philadelphia; Philip H. Heersema, Rochester, Minn.; Erich Lindemann, Boston; Edwin James Palmer, San Antonio, Texas; Joseph Pessin, Madison, Wis.; Paul William Preu, New Haven, Conn.; Frederick Carl Redlich, Boston; Max Rinkel, Boston; Jurgen Ruesch, Boston; Manuel Sall, Philadelphia; Irving C. Sherman, Chicago; Carl Sugar, New York; Martin Lee Towler, Denver; Maurice N. Walsh, Rochester, Minn.; Edwin A. Weinstein, New York; Hyman E. Yaskin, Camden, N. J.

Neurology and Psychiatry.—On Record: Rubin A. Gerber, New York; Max Gruenthal, New York; Frederick Hiller, Chicago; Paul Bernhard Jossmann, Boston; James Francis McDonald, New York; Richard H. Price, Guantanamo Bay, Cuba; Andrew I. Rosenberger, Milwaukee, Wis.; R. Montfort Schley, Buffalo; George Max Schlomer, Georgetown, Mass.; Leslie Bennet Sims, Medical Lake, Wash.; Henry Valentine Wildman, New York; George Wilson, Philadelphia.

THE AMERICAN BOARD OF NEUROLOGICAL SURGERY

At a meeting of the American Board of Neurological Surgery held in New York, May 12 and 13, 1942 the following diplomates were certified:

Eldridge Campbell, Albany, N. Y.; Francis A. Carmichael, Kansas City, Mo.; Francis A. Echlin, New York; Theodore C. Erickson, Madison, Wis.; William T. Grant, Los Angeles; Everett G. Grantham, Louisville, Ky.; W. Tracy Haverfield, Jacksonville, Fla.; Franklin Jelsma, Louisville, Ky.; Abraham Kaplan, New York; John Martin, Chicago; Russell Meyers, Brooklyn; J. Lawrence Pool, New York; Bronson Sands Ray, New York; Henry G. Schwartz, St. Louis; Joseph H. Siris, Brooklyn; James C. White, Boston.

ILLINOIS PSYCHIATRIC SOCIETY

At the annual meeting of the Illinois Psychiatric Society held on May 9, 1941, Dr. Francis J. Gerty was elected president, Dr. Franz Alexander vice president and Dr. Eugene I. Falstein secretary-treasurer.

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Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Anatomy and Embryology

THE RESPONSES OF CATFISH MELANOPHORES TO ERGOTAMINE. G. H. PARKER, Biol. Bull. **81**:163, 1941.

It is now known that the so-called contraction of catfish melanophores is the result of a neurohumor from the concentrating nerve fibers, very likely epinephrine, and that their expansion is due to two agents, intermedin from the pituitary gland and a neurohumor, probably acetylcholine, from the dispersing nerve fibers. In consequence of these new discoveries it seemed desirable to repeat Bacq's experiments with the view of bringing his rather remarkable results into relation with this newly acquired information.

Experiments on 15 catfish showed that ergotamine acts only on innervated melanophores by inducing them to disperse their pigment. It is without effect on denervated melanophores either with dispersed or with concentrated pigment. It acts on innervated melanophores only indirectly, that is, through their nerves. These are excited by ergotamine centrally to produce at their melanophore terminals acetylcholine, which causes the color cells to disperse their pigment. Ergotamine is a good example of an indirect excitant of melanophores, as contrasted with direct excitants, such as intermedin, acetylcholine and epinephrine, all of which act directly on the color cells.

COBB, Boston.

THE LOCI OF OLFACTORY END-ORGANS IN THE BLOWFLY, CYNOMYIA CADAVERINA DESVOIDY. HUBERT FRINGS, J. Exper. Zool. **88**:65 (Oct.) 1941.

Blowflies, Cynomyia cadaverina Desvoidy, were attached to blocks of beeswax on the ends of glass rods. They were then conditioned to the odor of coumarin (contained in a weighing bottle) by immersing their tarsi in a sugar solution and allowing them to feed during exposure to the coumarin. Extension of the mouth parts (proboscis response) later served as an indicator of the association of the odor with feeding. After conditioning various operations were performed, and the flies were tested in order to discover the location of the olfactory organs. Antennectomy, labellectomy, palpectomy, tarsectomy, coating the head capsule with lacquer and various combinations of these procedures were employed. It was found that the antennae and the labella are the sole bearers of olfactory end organs in the blowfly. No sex differences with respect to learning or olfaction were discovered. It is suggested that the antennal organs may serve as directional distance chemoreceptors involved chiefly in orientation, while the labellar organs function only during feeding.

WYMAN, Boston.

HISTOLOGICAL ALTERATIONS IN DENERVATED NON-REGENERATING LIMBS OF URODELE LARVAE. ELMER G. BUTLER and OSCAR E. SCHOTTÉ, J. Exper. Zool. **88**:307 (Nov.) 1941.

Larvae of three species of urodeles, Amblystoma punctatum, Amblystoma opacum and Triturus viridescens, were used. One forelimb in each larva was maintained in a nerveless condition by repeated resections of the brachial plexus, while the other was allowed to retain its innervation. Both limbs were amputated, and subsequent changes in them were studied microscopically and compared. Various levels of amputation were employed in different specimens. Cellular dedifferentiation of all tissues proceeded in nerveless limbs from any level of amputation proximally to the head of the humerus. No blastema was ever established on a completely nerveless amputated limb, but one was established when

reinnervation of a dedifferentiating limb took place. The point where such a blastema originated had no direct relation to the time or to the level of amputation. Regeneration was not possible in the absence of a blastema. The blastema seems to be related not only to the establishment of a regenerate but to the balance between the processes of dedifferentiation and differentiation, which are associated in regeneration.

WYMAN, Boston.

VASCULARIZATION IN THE BRAINS OF REPTILES: II. THE CEREBRAL CAPILLARY BED IN SPHENODON PUNCTATUM. E. HORNE CRAIGIE, J. Morphol. **69**:263 (Sept.) 1941.

Examination of serial sections of 2 Sphenodon brains revealed that the blood vessels are arranged entirely in pairs. Each member of a pair is usually branched, the branches culminating in a hairpin loop which connects the two components of the pair. The cerebral capillaries are of greater caliber and the erythrocytes are larger than those in the brain of any other reptile thus far studied. The vascularization of the brain, however, is relatively poor, that of the trigeminal centers and the cerebellum being particularly poor. The cochlear nucleus is the richest part studied. The observations suggest a low rate of metabolism in Sphenodon. Sphenodon is the sole living representative of the Rhynchocephalia and is supposed to be close to the main stem of reptilian descent. The arrangement of the cerebral vessels suggests that stem reptiles had a cerebral capillary bed of the loop type, similar to that possessed by the majority of lizards.

WYMAN, Boston.

Physiology and Biochemistry

THE EFFECT OF TEMPERATURE ON THE DEVELOPMENT OF FORM AND BEHAVIOR IN AMPHIBIAN EMBRYOS. G. P. DUSHANE and CRANFORD HUTCHINSON, J. Exper. Zool. **87**:245 (July) 1941.

Two series of eggs of Amblystoma punctatum were allowed to develop at two constant temperatures, 11 and 20.5 C., respectively. The behavior reactions during Harrison's morphologic stages 32 to 39 were studied at the two temperatures. There were highly significant differences in the two series. The frequency of advanced patterns of activity at any given stage of external development was relatively less in the cold series, and the frequency of less advanced behavior was relatively greater. Apparently, low temperature retards the development of behavior. The development of form and the development of behavior were differentially affected by changes in temperature, the latter being inhibited more by low temperature than was the former.

WYMAN, Boston.

MORPHOLOGICAL EFFECTS OF DENERVATION AND AMPUTATION OF LIMBS IN URODELE LARVAE. OSCAR E. SCHOTTÉ and ELMER G. BUTLER, J. Exper. Zool. **87**:279 (July) 1941.

Larvae of Amblystoma punctatum, Amblystoma opacum and Triturus viridescens, from 16 mm. to 55 mm. in length, were used. One forelimb of a larva was maintained nerveless for several weeks by removing the brachial plexus and resecting it every eight to ten or ten to twelve days. Amputation of the two forelimbs was performed simultaneously at the same level, and the regeneration of and subsequent morphologic changes in the two limbs were studied and compared. The denervated limb lost its capacity for regeneration but regained it as soon as it was reinnervated. The structures of the nerveless amputated limb underwent regression and resorption, the process proceeding proximally. This regression often results in disappearance of all formed structures of the limb and eventually of the limb itself. Articulations did not serve as barriers to the regressive processes, as many

as fourteen skeletal elements regressing after amputation through the metacarpals. Unamputated, nerveless limbs exhibited slight atrophy but no regression of structures. It was concluded that withdrawal of nervous influences disturbed the equilibrium of the sequence of cellular reactions on which regeneration depends. The nervous system not only exerts a trophic influence over cellular activities at the level of amputation but influences the organism as a whole in the processes responsible for regeneration.

WYMAN, Boston.

NEURAL DIFFERENTIATION WITHOUT ORGANIZER. L. G. BARTH, J. Exper. Zool. **87**:371 (Aug.) 1941.

Explants of the ectoderm of the gastrula of Amblystoma punctatum (stage 11) formed neural tubes in the absence of the organizer. The size of the explant, the region from which it was made and its orientation influenced neural differentiation. Small fragments which included only presumptive epidermis formed neural tubes. The frequency of differentiation increased when the anteroposterior axis of the explant was preserved. The neural tubes were formed from cells of the anterior end of the explant, which was located at or near the animal pole of the gastrula. It is concluded that a polarity, or gradient, for neural differentiation exists in the ectoderm, extending from the animal pole over the ventral surface of the gastrula into the vegetal hemisphere, with the other pole at the vegetal pole. The relation of this gradient to the action of the organizer is probably a reciprocal one, so that differentiation depends on a balance between the two.

WYMAN, Boston.

ON THE ULTRASTRUCTURE OF THE NEURAL PLATE AND TUBE OF THE EARLY CHICK EMBRYO, WITH NOTES ON THE EFFECTS OF DEHYDRATION. LAWRENCE B. HOBSON, J. Exper. Zool. **88**:107 (Oct.) 1941.

Whole chick embryos and isolated parts of them were examined with a Leitz petrologic microscope. The neural tube showed measurable birefringence, positive with respect to the long axis of the cells. Both form and intrinsic birefringence were present, principally in the plasma and nuclear membranes. The cytoplasm was also weakly anisotropic and showed the metatropic reaction. Similar birefringence was seen in the neural plate as observed from the side. There were no significant changes in the birefringence of neural structures during fold closure. Various non-neural structures also were birefringent. The results of experiments on dehydration of the embryo by concentrated solutions of salt or glycerin suggested that fold closure is the result of a differential imbibition of water by the neural plate.

WYMAN, Boston.

THE EFFECTS OF ALCOHOL UPON THE ELECTROENCEPHALOGRAM (BRAIN WAVES). PAULINE A. DAVIS, FREDERIC A. GIBBS, HALLOWELL DAVIS, WALTER W. JETTER and LOWELL S. TROWBRIDGE, Quart. J. Stud. on Alcohol **1**:626 (March) 1941.

Davis and her coauthors state that the electroencephalogram is modified in cases of acute alcoholic intoxication. Previous experience has shown that any condition which modifies the level of consciousness or of physiologic activity also produces a concomitant change in the pattern of the electroencephalogram. The authors feel that their most striking results are the demonstrations that electroencephalographic patterns of persons with chronic alcoholism (without alcohol) are not particularly abnormal and that the patterns of average young men in a state of acute intoxication are nearly nonrmal.

Psychometric tests were given to the same group, which consisted of 6 subjects whose ages ranged from 22 to 25 years, and the alcohol content of the blood was

measured. While the concentration of alcohol in the blood was at its height (125 to 140 mg. per hundred cubic centimeters) and for an hour thereafter, the subject's performances on the psychometric tests and his strength of grip were definitely impaired. The blood alcohol was still elevated (90 to 120 mg. per hundred cubic centimeters) and the modifications of the electroencephalogram were still prominent at the end of the experiment, after the subject was fairly sober. At higher concentrations of alcohol in the blood episodes of slow waves (4 to 8 cycles per second) intruded into the subject's characteristic electroencephalographic pattern and appeared in the spectrum analysis as an increase of energy in the corresponding frequency band.

The occurrence of these episodes of slow waves in the electroencephalogram became prominent when the subject's muscular tone and coordination diminished. When the subject later became lethargic, the electroencephalographic changes were not like those in sleep, but more nearly resembled those seen when a subject breathes a low oxygen mixture.

The electroencephalograms of 15 nonpsychotic patients who were confined in mental disease hospitals because of chronic alcoholism were found to lie between the range of the normal control group and that of psychotic patients in the same hospital.

BRACELAND, Chicago.

CONVULSIVE REACTIVITY IN HYPERCHOLESTEREMIA. E. SPIEGEL and H. WYCIS, Confinia neurol. **3**:262, 1941.

Spiegel and Wycis state that hypercholesteremia, produced in rabbits by various means, failed to decrease the convulsive reactivity of the brain. They express the belief that a comparison of this result with the protective influence of cholesterol against convulsive toxins demonstrates the importance of an examination of the convulsive reactivity by direct stimulation of the brain in any study of anticonvulsant agents.

DEJONG, Ann Arbor, Mich.

Psychiatry and Psychopathology

A STUDY OF SERUM PROTEINS IN MENTAL DISEASE. A. A. KONDRITZER and S. E. BARRERA, Psychiatric Quart. **15**:336 (April) 1941.

The solubility-precipitation pattern of the serum proteins of a group of schizophrenic patients was determined. The procedure consisted of the precipitation of the proteins by equimolar solutions of potassium biphosphate (KH_2PO_4) and potassium phosphate (K_2HPO_4) in serial concentrations ranging by 0.1 mol increments from 1.2 to 3.0 mols. In this way patterns of precipitation could be observed. The patterns found immediately before and after metrazol convulsions were found to be the same in all 6 cases. However, after the convulsions there was an increase of 0.6 per cent in the concentration of total serum protein. The results for 7 patients under insulin coma therapy were found to be the same as those for 6 untreated schizophrenic patients. The results for the 13 patients mentioned were compared with those for 6 healthy controls. No differences in the patterns were noted, but the total protein precipitated from the serums of the schizophrenic patients averaged 2.5 per cent less than the concentrations found for the control subjects. This finding was statistically analyzed and was deemed significant.

SIMON, Worcester, Mass.

A CRITICAL ANALYSIS OF INSULIN THERAPY AT ROCHESTER STATE HOSPITAL. W. LIBERTSON, Psychiatric Quart. **15**:635 (Oct.) 1941.

Libertson compared the status as of January 1941 of 165 schizophrenic patients who had been treated with insulin and that of an equal number of contemporary, randomly selected schizophrenic patients not treated with insulin. The condition

of the patients at the end of periods ranging from seven months to nearly four years was evaluated. The control group for the most part comprised patients deemed unfavorable subjects for insulin therapy. The results in both groups were essentially the same and agreed with statistics in the literature for schizophrenic patients not receiving any specific therapy. The results at the termination of treatment were more favorable but less permanent.

SIMON, Middletown, Conn.

AN IMPORTANT FACTOR IN EATING DISTURBANCES OF CHILDHOOD. EDITHA STERBA, Psychoanalyt. Quart. **10**:365, 1941.

Sterba cites 2 cases in which feeding disturbances occurred in very young children as an expression of conflict over toilet training. In both cases the feeding difficulty disappeared as soon as the demands for toilet training were relaxed for a time. These observations have an important practical bearing on the understanding and treatment of eating disturbances of childhood.

PEARSON, Philadelphia.

TOTAL GASTROSPASM. E. GRANET, Psychosom. Med. **2**:17 (Jan.) 1940.

Granet describes the case of a woman who had an acute stomach disorder in the form of total gastrospasm, which was confirmed by roentgen study. Complete relief of symptoms followed adequate sedation, and a roentgenogram of the stomach within twenty-four hours revealed no spasm. From a psychiatric standpoint the patient's personality was regarded as like that described by Alexander as characteristic of gastric dysfunction. Facts are presented suggesting that the patient within a short period was exposed to highly emotional situations, which probably enhanced deep oral receptive drives. These unconscious forces, previously repressed by the ego, achieved expression regressively in the form of a gastric neurosis, the gastrospasm.

SCHLEZINGER, Philadelphia.

OBESITY IN CHILDHOOD: V. THE FAMILY FRAME OF OBESE CHILDREN. H. BRUCH and G. TOURAINE, Psychosom. Med. **2**:141 (April) 1940.

Bruch and Touraine report in detail their investigation of 40 families from which obese children have come to their clinic. This report is restricted to a presentation of the influence of the parental environment on the development of the obese child. They note that although the economic level of these families is marginal, the condition of the homes is good. The amount of money spent for food is relatively large. Many of the fathers appear to be weak and submissive, with little ambition. The mothers have usually suffered from poverty and insecurity in childhood, reacting with self pity and resentment. Marital disharmony expresses itself in overt struggles or contempt. With few exceptions, the mothers have had the dominant parental role. The families are conspicuous for their small size. The attitude of mothers toward their obese children shows a marked ambivalence, with compensatory overprotectiveness and excessive feeding. In the child-parent relationship, food emotionally represents love, security and satisfaction. The parents hesitate to withhold food, while, on the other hand, they tend to consider muscular activity as a danger and threat.

SCHLEZINGER, Philadelphia.

SCHIZOID PERSONALITY AND SCHIZOPHRENIA. LEO H. BARTEMEIER, War Med. **1**:675 (Sept.) 1941.

Bartemeier calls attention to the fact that physicians who examine draftees must recognize that full-blown cases of schizophrenia will seldom be found among drafted men. Instead, they must be prepared to recognize the subtler abnormalities, which may represent the earliest manifestations of schizophrenia. Many lay

persons and physicians believe that the discipline and regularity of army life will snap certain young men out of their shyness and their day dreaming. In reality army life will tend to increase these tendencies.

The success of the psychiatric interview in forming opinions as to the draftee's mental health depends on the attitude of the psychiatrist toward the draftee. If the examining psychiatrist receives the registrant with interest, with regard for his immediate situation and without insisting on replies to his questions, he may obtain what information he needs.

Psychiatric experience has demonstrated that the first intuitive impression of a registrant may be entirely erroneous. The psychiatrist needs to note, first, the manner in which the registrant responds during the examination, second, what he says about himself and, finally, any dissociated phenomena which he manifests. Because of the brevity of the examination, unwitting activity, such as localized tensions or contractions, deserve especial emphasis because they are trustworthy indicators of internal stress. They are especially valuable if they happen to be elicited in connection with a specific topic about which the registrant is talking. The registrant may react strangely to the existence of some minor physical discrepancy or defect, and this may be the only clue to his prepsychotic state other than the vague impression he gives of being somewhat queer. This fact shows how important it is to attempt to find out in each instance what the registrant thinks about himself. If the physician on the local draft boards would, in the course of their examinations, ask each registrant what he thinks about this or that physical irregularity, a much larger number of mentally sick persons than are now being recognized could be spared the development of a later psychosis by being prevented from entering the service. The schizoid personality is not a well defined clinical entity like depression, hysteria or hypochondriasis. Many schizoid men give the impression that they are queer, cold, indifferent and distant. In them the condition is not difficult of recognition. With others, however, one does not sense anything abnormal. They seem to be good mixers, appear friendly and display considerable aggressiveness. They get along well socially and often hold responsible positions in the community. The one essential characteristic of the schizophrenic person, however well he may use his remarkable gifts or conceal them, is that he suffers from his fellow man more than the normal person can imagine. If the psychiatrist is alert, if he does not assume that he is to his registrant what he believes himself to be, then he may notice the telltale evidences of tension, the signs of caution and the obscure misunderstandings that are the hallmarks of the schizoid person's preternatural effort to make out exactly what the psychiatrist is and precisely what the situation means or implies. If the psychiatrist is bored or annoyed by persons who take life with this preternatural seriousness, then all that can be suggested is that he suspect of being schizoid every one who obscurely annoys him. He will be acting with the same unrecognizable scrutiny which psychiatrists have to accord to all persons who have significant roles with them. If the psychiatrist is not of this so-called normal extrovert type, then he may well look closely at every registrant in the procedure of whose examination something has struck him as being odd or unusual. If he is so diligently devoted to his work that he questions these interesting people and if he finds, although the registrant has every apparent intention of informing him, that his replies increase his puzzlement, then he may well consider that he is dealing with a schizoid person. The final test can be made if the psychiatrist arranges a private interview with the registrant and inquires by a matter-of-fact and natural series of questions that explore the relations of the registrant with schoolmates, fellow workers, friends and acquaintances; he may then confirm the diagnosis when he discovers that none of the man's relations are commonplace and conventionally routine; every one who means anything to him means a good deal. The schizoid person is a person who exhausts himself with the intricacies of his personal relations.

PEARSON, Philadelphia.

Meninges and Blood Vessels

CEREBROSPINAL FEVER AMONG BRITISH TROOPS IN FRANCE. R. PRIEST, J. Roy. Army M. Corps **76**:249 (May) 1941.

Priest states that 204 cases of cerebrospinal fever occurred between February 1940 and June 14, 1940 in the British Expeditionary Force in France. The diagnosis in 171 cases was proved bacteriologically, and the symptoms, physical signs, clinical course and general characteristics of the cerebrospinal fluid in the other 33 cases were typical. At no time was the infection epidemic. In fact, its sporadicity was a particularly conspicuous feature. The onset was varied and deceptive. It was of three types: the severe fulminating type, with rapid loss of consciousness and late meningeal signs; the more usual acute onset, with immediate signs of meningitis, and the type with chronic meningococcic bacteremia. The onset in 56 cases was sudden. In 12 the illness followed some form of exercise or exertion. Rigor, headache, vomiting and nuchal stiffness were the most frequent symptoms in all stages of the disease. Vomiting was sometimes troublesome and persistent. It was absent throughout the illness in 17 cases. A few patients did not vomit until treatment with sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine) was begun. Pain and stiffness in the neck and headache were steadily progressive. Photophobia was a fairly common symptom late in the disease. At first some patients were treated with sulfapyridine and antimeningococcus serum, but experience showed that the response to chemotherapy alone of patients suffering from the severe and fulminating forms of the disease was excellent and rapid. Thereafter administration of serum was discontinued. In fact, the serum sickness of a few patients proved to have a "nuisance value" and to be a check to an otherwise uneventful convalescence. The maximal dose of sulfapyridine was 81 Gm. in ten days, and the minimal dose was 14.5 Gm. in six days. The average dose per patient was 34.4 Gm., administered during seven and nine-tenths days. Cyanosis was a frequently observed feature during therapy, but it was never of sufficient intensity to justify discontinuing treatment. The rapid amelioration of the patients' general condition was little short of miraculous. The comparative absence of permanent disability was another welcome feature. From a military aspect sulfanilamide and its derivatives have proved of inestimable value in that once a patient is under the influence of the drug he can be moved from a forward unit to one farther back by ambulance or train, or overseas, without detriment to recovery. Chemotherapy permits the sending of convalescents to a convalescent depot instead of on sick leave. Of 50 men sent to a convalescent depot in France, 46 were examined at intervals and only 3 claimed to have annoying headaches; 1 or 2 complained of pain at the site of lumbar puncture, but, aided by the example of the others, they got well and went back to duty. There were 2 deaths, but neither was due to the effects of the meningococcus: One patient died six weeks after onset from an ascending infection following repeated catheterization, and the other died of bronchopneumonia and pericarditis with effusion and adhesions not of meningococcic origin.

J. A. M. A.

MENINGOCOCCAL INFECTION, WITH SPECIAL REFERENCE TO MENINGOCOCCAL SEPTICEMIA. G. C. MOSS, M. J. Australia **1**:548 (May 3) 1941.

Moss states that failure to obtain organisms in blood cultures is of no significance when typical signs and symptoms of meningococcic septicemia are present. Treatment should not be withheld too long. More widespread knowledge of the significance of the typical rash in conjunction with other symptoms will lead to a diagnosis in many cases at the first examination. This is of great importance today, as sulfapyridine (2-[paraaminobenzenesulfamido]-pyridine) is capable of bringing about a speedy cure. This prompt therapeutic response is an additional diagnostic feature. Results with sulfapyridine in treatment of meningococcic meningitis have been spectacular, and it was to be expected that they would be even better in cases of the slow forms of septicemia without meningeal localization. A disease that may entail weeks or months of illness and may end in meningitis,

or even meningococcic endocarditis with or without other complications, can scarcely be called benign in spite of a strong tendency to spontaneous cure. For immunologic reasons more cases are likely to be encountered in the later stages of an epidemic. Moss's first case was one of chronic meningococcic septicemia, lasting at least thirty-three days and terminating in meningitis. Progress was uninterrupted except for nausea from use of the sulfapyridine. The patient was allowed up on the fourteenth day and at the time of writing is quite well. The second patient was treated with sulfapyridine for six days, receiving a total of 23 Gm. of the drug. Thirteen days after chemotherapy was instituted examination of a nasopharyngeal swab did not reveal Neisseria meningitidis. The onset of subacute and chronic forms of meningococcemia is usually, but not invariably, sudden, with malaise, shivering, pains in the limbs, especially the legs, and recurrent headache, of varying intensity. This is true also of meningeal signs. Pain in the extremities is not necessarily confined to joints; a joint effusion may or may not be present. With the shivering and rise of temperature there may be a profuse cutaneous reaction and attendant discomfort; yet the patient may feel quite well with the fall of temperature. This comparative well-being has impressed most of those who have seen such patients. The temperature may resemble that of malaria, or it may be of the common septic type. The rash of meningococcemia, once seen, is not likely to be forgotten. Minor variations exist, but in general the same basic pattern is present. The lesions consist of pink or red macules and papules varying from a pin's head to a threepenny piece in size; a few larger lesions are often present. The smaller ones are roughly circular; the larger ones are often longer than they are broad. The large ones are usually tender. The limbs are usually most affected, but lesions are commonly seen on the back and chest, sometimes on the abdomen and more rarely on the face. The color may be uniform or the center more vivid. Complete disappearance with pressure is the rule, except when there is a petechia in the center. Isolated petechiae may coexist. Tender papules or nodes may be found on the shins. They may be confused with erythema nodosum or erythema multiforme. The lesions usually fade in a day or so, some completely, or a faint brown stain from some may persist for several days. At intervals, often corresponding with the presence of fever, other lesions may appear. Herpes labialis carries as much diagnostic weight as it does in meningitis.

J. A. M. A.

MENINGOCOCCIC INFECTIONS. W. GOETERS, Monatschr. f. Kinderh. **87**:144 (March 24) 1941.

Goeters reports observations on 138 children with epidemic meningitis. Pathogenic organisms were detected in 87 per cent; many of the meningococcus strains were facultative anaerobes. Simultaneous aerobic and anaerobic culture, particularly after preliminary enrichment in ascitic bouillon, improves the results of the culture method. The demonstration of causal organisms in the cadavers of children who died of meningococcic infection was more successful in cultures of material from sternal marrow than in those of the heart blood. The sporadic cases of meningitis have the most unfavorable prognosis. The mortality rate decreases in the course of an epidemic, and this must be taken into consideration in evaluating treatment. Type determination suggests that this decrease in mortality rate during an epidemic is due partly to a decrease in the virulence of the pathogenic organism. Thus, whereas type I caused severe forms of meningitis in 1939, it caused mild disease in 1940. In an epidemic caused by type VI, the first cases were usually of severe and fatal meningitis, but later the same type caused only abortive forms. Serums, repeated blood transfusions, insufflation of air into the lumbar sac and irradiation failed to exert a therapeutic effect. Sulfanilamide and azosulfamide were ineffective, but sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine) proved highly successful. Early exhibition and large initial doses are decisive for the efficacy of sulfapyridine in meningococcic infections.

J. A. M. A.

Diseases of the Brain

HUMAN EQUINE ENCEPHALOMYELITIS IN KERN COUNTY, CALIF., 1938, 1939 AND 1940. W. C. BUSS and BEATRICE F. HOWITT, Am. J. Pub. Health **31**:935 (Sept.) 1941.

Buss and Howitt state that since 1939 a different point of view has obtained concerning the neurotropic diseases (equine encephalomyelitis and poliomyelitis) in Kern County, Calif. Although poliomyelitis predominated, an unexpectedly high proportion of the cases were of equine encephalomyelitis and a few were of the St. Louis type of encephalitis. This was demonstrated by serum neutralization tests. In a few cases the type remained undiagnosed. Thus it has been shown that more than one variety of neurotropic virus disease is prevalent in the county. In 1938, 71 patients; in 1939, 160 patients, and in 1940, 85 patients were admitted to the Kern County General Hospital with a tentative diagnosis of neutrotropic virus disease. On the basis of neutralization tests, epidemiologic histories and clinical and laboratory observations 116 patients were segregated as having equine encephalomyelitis—22 in 1938, 46 in 1939 and 48 in 1940. The western equine virus was recovered from the brains of 2 patients. Of 112 specimens of serum obtained during the three years from patients with a diagnosis of encephalitis 97 (86.6 per cent) neutralized the equine virus and of 82 specimens of serum from patients with a diagnosis of poliomyelitis 5 (6 per cent) likewise neutralized the virus. Among 82 well contacts, the serum of only 6 (7.3 per cent) showed evidence of neutralizing ability; the serum of 5 was weakly positive and that of 1 was strongly positive. The serum of 29 (70.7 per cent) of 41 sick contacts tested for neutralizing ability was positive for the virus of equine encephalomyelitis. That so many of the sick contacts really had a mild form of the disease is suggestive of a common source of infection or of exposure to similar environmental conditions, especially as many of the patients lived on farms, in labor camps, in box cars or in small towns where there was an abundance of mosquitoes. Males were predominant among patients with poliomyelitis or encephalitis, and the largest percentage of patients with a diagnosis of encephalomyelitis in all three years were children less than 10 years of age. Equine encephalomyelitis began about May, increased to a peak in August in 1938 and 1939 and in July in 1940 and then dropped off abruptly, with only a few cases through November. All cases were centered in the farming and irrigated areas in the central and western portions of the county. None was reported from the mountains or the eastern desert districts. Treatment during the acute and subsequent stages of the disease was entirely nonspecific. For severe convulsions a variety of sedatives were used. During the comatose state fluids were given parenterally, and gavage feedings were administered as required. Small transfusions and intramuscular injections of blood were given routinely. Physical therapy or casts were used for spasticity or weakness of the extremities. A periodic check of every patient followed discharge from the hospital. All of them apparently had a normal recovery. That 97 patients with encephalitis in Kern County during the last three years have given positive neutralization reactions to the western equine virus suggests that a permanent endemic area will exist unless control measures are instituted.

J. A. M. A.

MUMPS ENCEPHALITIS. W. L. DONOHUE, J. Pediat. **19**:42 (July) 1941.

Donohue reviews the micropathologic picture of mumps encephalitis as it is reported in the literature, finds that the reports do not follow a set pattern and that the changes described in the case of Bien and Wegelin are similar to those in his case. He believes that these 2 cases are the only ones in which the micropathologic changes are adequately described and in which there can be no doubt that encephalitis complicated mumps. The lesions in his case, although funda-

mentally identical with those found in the central nervous system in the encephalitides following other infections (smallpox, chickenpox or measles) and vaccination, were not as severe. The fundamental lesion was perivascular demyelination. If the lesions had not been so widespread or if pulmonary complications had not been present, recovery might have taken place. No virus studies were done on the tissues obtained.

J. A. M. A.

DIAGNOSIS AND TREATMENT OF SUBDURAL HEMATOMAS. H. C. VORIS, Surgery **10**:447 (Sept.) 1941.

Voris discusses a series of 35 consecutive cases of subdural hematoma in which operation was performed with a mortality of 43 per cent. The mortality was 24 per cent (9 patients) for those operated on more than three days after injury. Clots were removed in 34 cases, and in 1 the clot was not found on the side indicated by the neurologic signs and the other side was not explored. Necropsy was performed by the coroner's physician on 5 of the patients operated on within three days; cerebral contusion or laceration was present in all. One of these was a patient with bilateral subdural clots who had two explorations a week apart and died of meningitis after the second exploration. Necropsy was performed on 5 of the 6 patients who died and had been operated on more than three days after injury. One of these had an unrecognized clot on the side opposite that explored. The other 4 had pulmonary pathologic changes of bronchopneumonia or pulmonary abscess thought to be the cause of death. The mortality was very high (9 of 10 patients) among patients with acute or early subdural hematoma, that is, with unencapsulated clots operated on within three days of injury. These clots are often associated with cerebral injury. The mortality is also high in old people. Chronic or late subdural hematoma in young or middle-aged persons without associated systemic disease has a good prognosis if operation is performed before increased intracranial pressure has rendered the patient moribund. Exploration should always be bilateral, especially if no clot is found on the side first explored. Two deaths in the present series occurred because this was not done. If the brain does not expand to fill the space previously occupied by the evacuated clot, measures such as filling the subdural space with distilled water to induce expansion must be instituted.

J. A. M. A.

TRAUMATIC LESION OF THE HYPOTHALAMUS. B. HORÁNYI-HECHST, Confinia neurol. **3**:266, 1941.

Horányi-Hechst describes the case of a woman aged 26 in whom changes in personality, loss of weight, insomnia, menstrual disturbances, lactation of the left breast, changes in distribution of hair and disturbances in pigmentation developed after an injury to the skull. Routine examinations, including encephalographic studies, gave normal results. It is stated that the changes noted may be explained by the assumption of a traumatic hemorrhagic lesion within the hypothalamic area.

DEJONG, Ann Arbor, Mich.

MANNERISMS AS AN ORGANIC MOTILITY SYNDROME (PARACORTICAL DISTURBANCES). LAURETTA BENDER and PAUL SCHILDER, Confinia neurol. **3**:321, 1941.

Bender and Schilder describe a group of cases in which there appeared to be a lesion of the subcortical motor apparatus or a change in the postural apparatus and in which stiffness, restless movements, clowning or mannerisms were seen. These disturbances in motility were noted in association with anoxia, administration of insulin, alcoholic encephalopathy, certain choreas and schizophrenia. The authors express the belief that these dyskinesias occur through an interaction of the subcortical influences and the total motor personality structure. They propose the term "paracortical disturbances" for these manifestations.

DEJONG, Ann Arbor, Mich.

NEUROLOGIC SYMPTOMS ASSOCIATED WITH MALIGNANT TUMORS OF THE RHINOPHARYNX. ERIK GODTFREDSEN, Acta psychiat. et neurol. **16**:47, 1941.

Godtfredsen reports on a series of 64 patients with malignant tumors of the rhinopharynx, of whom 25 (40 per cent) had neurologic symptoms. The commonest symptoms were those referable to involvement of the cranial nerves at the base of the brain within the skull. Of particular interest were 8 patients in whom trigeminal neuralgia developed early in the course of the disease. The author asserts that in every case in which trigeminal neuralgia appears early the patient should be specifically examined for the presence of cervical lymphadenopathy, which is of almost invariable occurrence with tumors of this type. Extensive and intensive roentgen irradiation is the treatment of choice. Of the 25 patients reported on, 3 were free from symptoms six to ten months, 2 for two to two and one-fourth years and 5 for six to eight and a half years after treatment.

BRENNER, Boston.

Vegetative and Endocrine Systems

CREATINE-CREATININE METABOLISM AND THE HORMONES. H. H. BEARD and P. PIZZOLATO, Endocrinology **27**:908 (Dec.) 1940.

Beard and Pizzolato report on the effects on creatine-creatinine metabolism of injection of pitressin, pitocin, desiccated thyroid, parathyroid extract, zinc insulin and insulin. After the injection of pitressin or pitocin there is retention of creatinine accompanied by a corresponding increase in excretion of creatine. The authors conclude that the retained creatinine is quantitatively transformed into creatine. That the increased creatine excreted is not obtained from the muscle creatine is indicated by the increase in muscle creatine following the injection of pitressin. Desiccated thyroid causes an increase in the excretion of creatine and creatinine in the normal and in the thyroidectomized animal. Thyroidectomy or injection of parathyroid extract was without appreciable effect. Zinc insulin caused a greater increase in the excretion of creatine and creatinine than did similar doses of insulin, possibly because of the zinc content of the former. With increasing doses of both preparations, there was observed a progressively decreasing excretion of creatine and creatinine.

PALMER, Philadelphia.

THE HYPOPHYSIS AND HEMOPOIESIS. O. O. MEYER, E. W. THWELIS and H. P. RUSCH, Endocrinology **27**:932 (Dec.) 1940.

As previously reported by the authors and others, hypophysectomy in rats produces reticulopenia, which is unaffected by parenteral injection of liver extract or by low oxygen tension but is relieved by the administration of a pituitary extract containing the growth hormone. These and other experiments have suggested the existence of a hypophysial hemopoietic hormone.

Further experiments are now reported which lead the authors to conclude that the effect of the hypophysis on hemopoiesis appears to be associated with general metabolic changes and probably is not dependent on a specific hormone acting on the bone marrow.

In hypophysectomized rats, reticulocytosis followed the injection of a pituitary preparation containing the growth-promoting hormone of the anterior lobe but not after the growth-stimulating factor was destroyed by boiling.

Thyroxin and preparations containing the thyrotropic and the adrenotropic principle of the anterior lobe produce reticulocytosis in hypophysectomized rats, and a significant increase in reticulocytes also followed the injection of nonspecific substances, such as ascorbic acid and a 5 per cent solution of sodium bicarbonate.

PALMER, Philadelphia.

THE EFFECT OF THE ADRENAL CORTEX ON CARBOHYDRATE METABOLISM. R. A. LEWIS, D. KUHLMAN, C. DELBUE, G. F. KOEPF and G. W. THORN, Endocrinology **27**:971 (Dec.) 1940.

The authors report on experiments which demonstrate that in adrenalectomized, phlorhizin-treated rats maintained by treatment with sodium chloride or desoxycorticosterone acetate there are (*a*) impairment in ability to form dextrose from lactic acid, pyruvic acid or alanine; (*b*) an increase in utilization of available dextrose, and (*c*) a decrease in ketonuria, glycosuria, nitrogen excretion and the dextrose: nitrogen ratio.

Adrenalectomized dogs maintained in electrolytic balance by treatment with desoxycorticosterone acetate were observed to have a decreased glycemic response to epinephrine, an increased sensitivity to insulin and a lowered threshold for signs of hypoglycemia induced by treatment with insulin or phlorhizin. All of these abnormalities were overcome by the administration of adrenal cortical extract or 17-hydroxy-11-dehydrocorticosterone.

The administration of corticosterone or adrenal cortical extract to adrenalectomized dogs resulted in a lowered respiratory quotient, increased nitrogen excretion and an increased level of dextrose in the blood.

The authors conclude that the administration of adrenal cortical extract or 17-hydroxy-11-dehydrocorticosterone restores the ability of adrenalectomized rats and dogs to resynthesize dextrose and glycogen from intermediate products of carbohydrate and protein metabolism and corrects the defects in carbohydrate metabolism.

PALMER, Philadelphia.

A COMPARISON OF THE BODY AND ENDOCRINE GLAND (ADRENAL, THYROID AND PITUITARY) WEIGHTS OF EMOTIONAL AND NON-EMOTIONAL RATS. E. H. YEAKEL and R. P. RHOADES, Endocrinology **28**:337 (Feb.) 1941.

The glands of rats which had been selectively bred for emotionality and nonemotionality, and which were bred and reared under uniform conditions, were carefully weighed by an identical procedure. Comparisons were made of the weights in groups of the same age and sex, and the female rats were killed during the diestrum, as determined by vaginal smears.

No significant difference was found in the body weights of comparable groups of emotional and nonemotional rats or in the weights of the pituitary glands of the male rats or of the adrenal glands of the female rats in the two groups.

Emotional male rats have heavier adrenal and thyroid glands. The weights of the thyroid, and especially of the pituitary gland, of emotional female rats were significantly higher than those of nonemotional female rats.

PALMER, Philadelphia.

VITAMIN B COMPLEX AND ADRENALECTOMY. W. G. CLARK, Endocrinology **28**: 545 (April) 1941.

Clark investigated the possible relationship between the vitamin requirements of adrenalectomized animals and the role of the adrenal cortex in the utilization of some of the members of the vitamin B complex. Other authors have proposed that adrenal insufficiency is in reality a secondary avitaminosis and have referred particularly to the necessity of the adrenal cortex for the phosphorylation and subsequent incorporation of riboflavin, thiamine and nicotinic acid into enzyme-coenzyme systems.

In controlled experiments Clark found that relatively massive but nontoxic doses of thiamine hydrochloride and cocarboxylase, administered parenterally and orally, exert no beneficial effects on the appetite, average daily loss of weight or survival of adrenalectomized rats maintained on a diet adequate for normal rats. There was no difference in the action of thiamine and that of cocarboxylase.

The same conclusion was reached in regard to riboflavin, the sodium phosphate ester of riboflavin, sodium nicotinate, pyridoxine and pantothenic acid. Other groups of adrenalectomized rats were given dietary supplements of a gross concentrate high in thiamine, riboflavin, nicotinic acid, factor W and the B_6 complex, and of a liver concentrate high in nicotinic acid, riboflavin, pantothenic acid and filtrate fraction, with no beneficial effects.

PALMER, Philadelphia.

THE ABOLITION OF MATING BEHAVIOR BY HYPOTHALAMIC LESIONS IN GUINEA PIGS. J. M. BROOKHART, F. L. DEY and S. W. RANSON, Endocrinology **28**: 561 (April) 1941.

Brookhart, Dey and Ranson had previously observed that properly placed lesions in the anterior part of the hypothalamus abolish estrual behavior in the guinea pig. One-half these animals ran normal cycles in respect to changes in the ovaries, the uterus and the external genitalia, so that the failure to show estrual behavior was not thought to be due to lack of estrogen. As further evidence in this direction, it was noted that spayed guinea pigs with similar lesions failed to respond to injections of estrogen in excess of amounts which had been sufficient to produce estrual behavior in the same animals before the hypothalamic lesions had been placed. Further experiments were designed to show whether the failure of the estrual behavior might be due to hormonal deficiency.

Animals with hypophysial lesions, some of them spayed, were given estrogen, a preparation of the pituitary containing the follicle-stimulating and luteinizing fractions or combinations of the two. In no case could estrual behavior be induced in the animals with hypothalamic lesions. The hypothalamic lesions have a specific effect, not produced by similar lesions placed 5 mm. higher in the brain. The authors conclude that this behavioral difficulty is probably due to impairment of a central mechanism for estrual behavior.

PALMER, Philadelphia.

THE EFFECT OF HYPOPHYSECTOMY UPON HYPERCHOLESTEROLEMIA OF DOGS. K. W. THOMPSON and C. N. H. LONG, Endocrinology **28**:715 (May) 1941.

Thompson and Long describe experiments designed to study the possible relationship of the anterior lobe of the pituitary gland to the hypercholesteremia associated with hypothyroidism. The hypercholesteremia of 7 thyroidectomized dogs was abolished by hypophysectomy. Adrenalectomy in 3 thyroidectomized dogs produced a similar effect. In 2 of the animals the results were difficult to evaluate because of the poor clinical condition of the animals. A marked and sustained elevation of the plasma cholesterol followed injections of crude sheep pituitary extract in 3 dogs. However, it was suggested that this result may have been an indirect effect, subsequent to the inactivation of the animal's thyroid glands by antihormones. In 1 of these dogs hypophysectomy was followed by a fall in the plasma cholesterol similar to that seen in the thyroidectomized dogs after hypophysectomy.

PALMER, Philadelphia.

THE PSYCHICAL ACTIVITY OF MALE AND FEMALE SEX HORMONES OF HORSE URINE. P. ENGEL, Endocrinology **28**:849 (May) 1941.

Although a reciprocal inhibitory action between androgen and estrogen is commonly found, the behavior of the stallion shows a vigorous male sexual instinct in spite of the presence of a very high quantity of estrogen in the urine and testes.

Engel found that normal sexual behavior in castrated male guinea pigs was not produced by the injection of 1 mg. of testosterone propionate or 2 cock comb units of a testicular extract (erugon), but did occur on the fifth day of daily administration of a crude benzene extract corresponding to 80 cc. of horse urine.

The same extract in the castrated female produced estrus and changes in the vaginal smears characteristic of the presence of estrogen.

It is noted that in this instance the presence of one "sex hormone" does not inhibit the activity of the other.

PALMER, Philadelphia.

ANTAGONISM BETWEEN THYROID AND POSTERIOR PITUITARY AND ITS RELATION TO THE AUTONOMIC NERVOUS SYSTEM. O. PECZENIK, L. POPPER and G. SCHMID, Confinia neurol. **3**:331, 1941.

Peczenik, Popper and Schmid state that experimental work has shown that the anterior lobe of the pituitary gland stimulates the thyroid gland and that the two glands influence each other mutually. They express the belief, however, that there is an antagonism between the posterior lobe of the pituitary and the thyroid gland. The effects of thyroxin and of the catabolic thyroid hormone have been inhibited by extracts of the posterior lobe of the pituitary gland, especially by pitressin. In the guinea pig this inhibiting effect can be prevented by the use of atropine. The authors conclude, therefore, that the posterior lobe of the pituitary gland produces parasympathetic stimulation, thus counteracting the increase in sympathetic tone brought about by thyroxin. Hyperthyroidism in man can be benefited by the use of extracts of the posterior lobe of the pituitary gland only when used in combination with other modes of therapy.

DEJONG, Ann Arbor, Mich.

Treatment, Neurosurgery

THE EFFECT OF NICOTINIC ACID IN STUPOR, LETHARGY AND VARIOUS OTHER PSYCHIATRIC DISORDERS. V. P. SYDENSTRICKER and H. M. CLECKLEY, Am. J. Psychiat. **98**:83 (July) 1941.

Sydenstricker and Cleckley used nicotinic acid in the treatment of severe, relatively acute psychotic states varying from stupor to an active psychosis. The 29 cases studied were mostly those of toxic psychosis or exhaustive delirium in which no adequate cause could be found, and in no case was there any clinical evidence of pellagra or other deficiency disease. The patients showed prompt, frequently dramatic, improvement after the administration of nicotinic acid. The drug was given intravenously in all but 6 cases. The total dose varied from 100 mg. to 30 Gm. The improvement in the clinical condition appeared within ten hours to six weeks. The authors recommend a therapeutic trial of nicotinic acid in treatment of patients presenting a picture of toxic psychosis or exhaustion delirium of unexplained origin. They concluded that this was the only available means for determining whether or not the psychosis is due to avitaminosis.

FORSTER, Boston.

ARTERIAL HYPERTENSION AND SECTION OF SPLANCHNIC NERVES. D. A. RYTAND and E. HOLMAN, Arch. Int. Med. **67**:1 (Jan.) 1941.

In choosing patients with arterial hypertension for splanchnic nerve section Rytand and Holman disregarded age, congestive heart failure, angina pectoris, coronary occlusion, hemiplegia and glomerulonephritis. Forty patients were subjected to operation. The results were generally poor; 8 died within two weeks of the operation, 11 within a year and a half, 5 had their blood pressure reduced to some degree, 6 felt better with no reduction in their hypertension, 9 experienced no change and 1 had a brilliant recovery. As early as three months after operation the heart of this patient was reported as normal in size. A year after operation the patient married. She now (three and a half years after operation, with a systolic pressure of 145 mm. and a diastolic pressure of 85 mm.) complains of fatigue and dyspnea only if she works hard but feels better while taking 0.1 Gm. of digitalis daily. There is no edema. While the symptomatic improvement

appeared at once, the main decline in arterial pressure did not occur until six months after operation. The average reduction of the arterial pressure of the 5 patients in whom it decreased was from 200 to 155 systolic and 120 to 100 diastolic. Their ages ranged from 30 to 54 years (average, 39 years). They were known to have been hypertensive for from two to ten years. None of these patients had any urinary abnormality or elevated blood urea concentration, and all but 1 had perfectly normal fundi. All had thickened radial arteries. One had survived an attack of coronary occlusion, and 2 presented themselves with congestive heart failure. Therefore age, duration of hypertension, vascular complications in the brain and heart, heart failure and lability of arterial pressure were not prognostically significant. The deciding prognostic factor seemed to be the presence or absence of malignant hypertension as evidenced by renal and retinal lesions.

J. A. M. A.

VITAMIN E IN TREATMENT OF MUSCLE DISORDERS OF INFANCY AND CHILDHOOD. S. STONE, J. Pediat. **18**:310 (March) 1941.

Stone used vitamin E in treatment of 2 children with pseudohypertrophic muscular dystrophy and 2 with congenital myotonia. After from three to six months of treatment there have been a striking formation of new muscle tissue, generalized increase in strength and sense of well-being. This has become apparent only since the children were placed on vitamin E. Only 1 of the patients has made a complete recovery. Through the facilities of the crippled children's and orthopedic clinics, the effect of vitamin E has been observed on a large group of children between 1 and 5 years of age who came to the clinic because of poor muscular development, inability to hold up their heads until they were 2 or 3 years old and retardation in beginning to stand or walk alone. The possibility that the muscle disturbances were caused by vitamin E deficiency in a lesser degree than is present in muscular dystrophies and myotonias prompted the addition of vitamin B complex and vitamin E to these children's diets. While the vitamin B complex tended to improve their appetites or produced increase in weight, the response in muscle strength was rather slow. When vitamin E in the form of wheat germ oil was added to the vitamin B complex the increase in muscle strength was more rapid. Usually within a month the mother reported that the child was able to stand better, hold up its head, turn over without assistance and attempt walking alone. An increase in mental alertness was observed in some of the children. Children with flaccid musculature responded much better than the group with spasticity. The dose for the dystrophic and myotonic groups was from 2 to 4 cc. of fresh wheat germ oil given daily, together with the vitamin B complex. In infants and young children with generalized muscular hypotonia the inital dose was from 8 to 12 minims (0.5 to 0.7 cc.) of wheat germ oil, preferably with the vitamin B complex. Deficiency in the mother during pregnancy, or her inability to transmit vitamin E to the offspring, is possibly a factor in the development of an impaired musculature of the newborn infant. Probably certain types of muscular dystrophy, some myotonias (Oppenheim) and, in certain cases, poor muscular development in the young infant are due to the same deficiency. This hypothesis is supported by the fact that vitamin E was of definite therapeutic value in cases of such disorders. As most children's diets are likely to be deficient in vitamin E, it is suggested that in certain obscure nervous and muscular disturbances of childhood vitamin E deficiency should be investigated as one of the causes.

J. A. M. A.

ELECTRIC SHOCK THERAPY IN STATE HOSPITAL PRACTICE. L. KALINOWSKY, N. BIGELOW and P. BRIKATES, Psychiatric Quart. **15**:450 (July) 1941.

The authors attempt a comparative clinical evaluation of electric shock therapy among patients in state hospitals. They accept the possibility of structural changes but attribute them to the convulsions, rather than to the treatment.

A study was made of 65 patients who were followed for two months after completion of treatment. All 5 patients with depressions of the manic-depressive type showed sustained remissions. Of the 7 manic patients, 5 had a remission, 1 improved and 1 failed to improve. One patient with a remission relapsed within two months. Definite changes occurred after three or four treatments. Six patients with involutional melancholia showed remissions irrespective of the duration of illness. Two with illnesses of three and four years' duration were treated, 1 of them being mute and requiring tube feeding before treatment was begun. Only 1 of 5 patients with involutional paranoia showed improvement after a course of twenty treatments. Forty-two schizophrenic patients responded to treatment, the results being in fair correlation to the duration of illness. Responses ranged from 8 remissions among 10 patients ill less than six months to failure of remission in all of 12 patients ill over two years (3 improved). Patients with old remitting disease presented somewhat better results, half of the 10 showing improvement or remission. The need for early treatment is emphasized. It is also noted that the unimproved patients showed much less assaultiveness and destructiveness. Of 56 patients treated for symptomatic effects, 42 (75 per cent) improved. No complications of the treatment occurred. Transient disturbances of memory cleared up.

SIMON, Middletown, Conn.

MODIFIED BULGARIAN BELLADONNA TREATMENT OF PARKINSONISM. L. REZNIKOFF, Psychiatric Quart. **15**:494 (July) 1941.

Reznikoff treated 14 patients having psychoses with postencephalitic parkinsonism for six months with a preparation of Bulgarian belladonna. The ages varied from 28 to 52 years. After the first three weeks placebos resembling the belladonna preparation were abruptly substituted for ten days. After nine weeks scopolamine, 1/100 grain (0.6 mg.) three times a day, was substituted for a month. All the patients were reported as responding to the treatment with belladonna better than to other methods of therapy. Oculogyric crises were less frequent, but were not abolished. The psychoses were not influenced in their essential structure but emotional instability improved. The author emphasizes individualization of treatment and recommends the use of adjuncts. These included scopolamine and phenobarbital for hyperkinesis and insomnia and amphetamine (benzedrine) sulfate for hypokinesis and hypersomnia. Psychologic, occupational and recreational therapies are stressed.

SIMON, Middletown, Conn.

THE USE OF "RABELLON" IN THE TREATMENT OF CHRONIC ENCEPHALITIS. C. W. HUTCHINGS, Psychiatric Quart. **15**:506 (July) 1941.

Hutchings studied 7 psychotic patients with a variety of chronic postencephalitic symptoms, all of more than ten years' duration. The study was carried out for nine months under as nearly standardized conditions as possible. Treatment with a mixture of alkaloids (hyoscyamus, atropine and scopolamine) was given in doses reaching pretoxic levels. All the patients had a period of rest from any treatment before receiving the preparation. During this period the symptoms generally increased. With the doses given uniform subjective improvement resulted. Objective changes were not noted, but the author expresses the belief that this treatment is the most effective yet found.

SIMON, Middletown, Conn.

SULFAPYRIDINE AS A PROPHYLACTIC AGAINST CEREBROSPINAL MENINGITIS. F. C. GRAY and J. GEAR, South African M. J. **15**:139 (April 12) 1941.

According to Gray and Gear, a bacteriologic investigation of an outbreak of cerebrospinal meningitis in a military camp in Natal revealed approximately 22 per cent of carriers among those examined, making conditions favorable for a widespread epidemic. As sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine)

is known to sterilize the cerebrospinal fluid of patients suffering from meningococcic meningitis within three days, it was thought that it might be equally effective in destroying the organisms in the nasopharynx of carriers. If this could be achieved a sudden diminution of the carrier rate would be expected and there would be an interval during which no further cases would occur. The carrier rate was determined on a sample population of the most severely affected battalion. Then all men of this battalion and carriers found in other units were given 2 tablets (1 Gm.) of sulfapyridine three times a day for two days. After one day the carrier rate among the sample population was again determined. As a control the carrier rate in an untreated battalion was also determined. Although 70 treated and only 43 untreated men were examined, no carriers were discovered among the treated men, but 10 were found among the untreated. Of still greater significance is the fact that 17 of the treated men were previously proved to be carriers. Under normal conditions, according to Flack (1917), about 20 per cent of contact carriers are infective for less than two weeks and the remainder for periods up to and for longer than twelve weeks. The carriers whose swabs yield a profuse growth of meningococci tend to be more persistent in their infectiveness. The majority of the carriers that the authors treated were of this type, and the results of their bacteriologic investigation have to a certain extent been confirmed by subsequent clinical observations and experience. In the month that has elapsed only 1 case of meningitis has occurred in the battalion treated, an officer who did not receive the treatment contracting the disease. A workman in the lines of this battalion who did not receive the prophylactic treatment died of meningitis. During this period several cases of meningitis occurred among the men of the control battalion until they, too, received the prescribed course of sulfapyridine. On the basis of their investigations Gray and Gear conclude that mass dosage is an efficient means of controlling immediately an epidemic of cerebrospinal meningitis by reducing the carrier rate to negligible proportions and preventing the onset of the disease in those in whom incubation occurs. The effect of the drug alone cannot be permanent, but they believe that by taking ordinary hygienic precautions the chances of a recrudescence of the disease in epidemic proportions is remote. They recommend that in the event of a case of cerebrospinal meningitis occurring in a semipermanent military camp the carrier rate should be determined if possible, and if it exceeds 20 per cent mass dosing with sulfapyridine is justified. The ordinary hygienic precautions must not be neglected.

J. A. M. A.

EMERGENCY SURGERY IN CEREBRAL ANGIOSPASM. B. V. BAPTISTA, Rev. méd. brasil. **9**:773 (Dec.) 1940.

According to Baptista, spasm of the cerebral vessels is caused by the disturbances in the nerve supply of the cerebral arteries due to sympathetic stimulation of the vasoconstrictive cerebral centers. The angiospasm may be mechanical or reflex. In either case it causes ischemia of cerebral tissue, with consequent infarction. It is likewise the cause of cerebral hemorrhage. Cerebral angiospasm does not subside spontaneously and constitutes an indication for urgent surgical intervention in order to improve the circulation about the ischemic zone in an attempt to prevent infarction. The author reports satisfactory results with procaine hydrochloride infiltration of the stellate ganglion, or with stellectomy, in 11 cases. He infiltrated the ganglion and the tissues about it with from 20 to 30 cc. of a 1 per cent solution of procaine hydrochloride. Stellectomy was performed by Leriche's technic. Either operation results in suppression of sympathetic stimuli and cerebral vasoconstriction, with consequent vasodilatation and normalization of the local circulation. In the 11 cases reported the results were satisfactory. Functional restitution in hemiplegia took place immediately after the operation.

J. A. M. A.

Encephalography, Ventriculography, Roentgenography

MISPLACED SPINAL LIPIODOL: AN ANALYSIS OF ONE HUNDRED AND FOUR LIPIODOL SPINOGRAMS. WALLACE B. HAMBY, Radiology **37**:343 (Sept.) 1941.

Hamby reviewed a series of 104 spinograms taken with iodized poppyseed oil and found the oil misplaced in the epidural or the subdural space in 8 cases, or in 7.7 per cent. In 91 lumbar injections it had been misplaced 5 times, or in 5.4 per cent, while in 13 cisternal injections it had been misplaced 3 times, or in 23 per cent.

Any factor tending to reduce the spinal fluid pressure predisposes to misplacement of the iodized oil. This statement is borne out by the results in 16 cases in which an air spinogram was followed at a short interval by lumbar injection of iodized oil, with 4 misplacements (25 per cent). This result occurred especially in patients with adhesive arachnoiditis.

Epidural iodized oil is visualized roentgenologically as a fairly fixed mass, which in a few days spreads out widely in the canal in the form of droplets and extends outward along the nerve roots. Subdural iodized oil, on the other hand, flows freely and does not become diffused. There is a tendency for the oil to outline defects which are not constant in serial examinations.

The author recommends that if a study with iodized oil is to be made after lumbar puncture or an air spinogram ten days be allowed to elapse between the procedures.

KENNEDY, Philadelphia.

THE ROENTGEN DIAGNOSIS OF NEURINOMA OF THE THORAX. I. N. ODESSKY, Radiology **37**:454 (Oct.) 1941.

Neurinoma of the thoracic wall is rare, Odessky being able to find only 1 case recorded in the literature which was similar to his.

Neurinoma of the posterior portion of the mediastinum is most common, 125 cases having been reported by Kienböck and Rösler in a review of the literature from 1870 to 1932. The appearance of thoracic neurinoma in the roentgenogram is that of a homogeneous shadow, semioval or spherical, with a distinct outline, which occupies in most cases the middle of the lung, with its base adjacent to the midthoracic portion of the spine. The size varies; it may be as large as an infant's head. A wide variety of conditions simulate this tumor: pulmonary tumor, teratoma, hydatid and other cysts, aortic aneurysm and encapsulated pleural exudates must be differentiated. There are no pathognomonic symptoms of neurinoma. Decisive factors in the diagnosis are the constancy of the roentgen picture and the good general condition of the patient. Neurofibromatous lesions in the skin and elsewhere are also confirmatory evidence.

The author reports 2 other cases with the more typical posterior mediastinal location. He believes that these tumors are more common than is supposed, partly because of their slow growth and lack of subjective symptoms.

KENNEDY, Philadelphia.

CEREBRAL ARTERIOGRAPHY WITH DIODRAST, FIFTY PER CENT. SIDNEY W. GROSS, Radiology **37**:487 (Oct.) 1941.

Gross reports that because of the dangers in the use of thorium dioxide this substance has been supplanted by the less toxic diodrast. A 70 per cent solution was first tried, but as this caused jacksonian seizures in 3 of 12 patients, a 35 per cent solution was substituted. Adequate visualization, however, was not obtained with this concentration. With a 50 per cent solution uniformly good visualization has been obtained and there have been no serious reactions.

The technic employed by Gross is as follows: 1. Five grains (0.325 Gm.) of soluble phenobarbital U. S. P. is given the patient one hour before the injection. 2. An incision is made parallel to and about an inch (2.5 cm.) above the clavicle on the side of the suspected lesion, with the use of local anesthesia, and the common carotid artery is exposed. 3. Preparations for obtaining a rapid exposure with the patient in the lateral position are made. 4. The common carotid artery is then punctured with a curved 17 gage curved needle having a rubber connection. 5. A syringe containing 15 cc. of 50 per cent diodrast is connected to the tubing, and 10 to 12 cc. is injected as rapidly as possible, the film being exposed during the injection. The exposure should not require more than a quarter of a second. A second injection may be carried out if stereoscopic views are desired. 6. Bleeding from the puncture wound usually stops promptly on the withdrawal of the needle, but occasionally pressure with a sponge soaked in warm saline solution may be required.

KENNEDY, Philadelphia.

CORRECTION

In the article by Drs. L. J. Meduna, F. J. Gerty and V. G. Urse entitled "Biochemical Disturbances in Mental Disorders" in the January issue (ARCH. NEUROL. & PSYCHIAT. **47**:38, 1942) the following corrections should be made: In the sixth and fifth lines from the bottom on page 42 "96.0 per cent" and "97.8 per cent" should read "96.0 mg. per hundred cubic centimeters" and "97.8 mg. per hundred cubic centimeters." In table 1, page 43, the fifth value in the one hour column should be "61" instead of "51," and the first total under the four hour column should be "713" instead of "1,713." In the first line on page 44 "6.79" should be "6.21."

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY, AND NEW YORK NEUROLOGICAL SOCIETY

GEORGE H. HYSLOP, M.D., *Chairman, Section of Neurology and Psychiatry, Presiding*

Joint Meeting, Nov. 11, 1941

Choreoathetosis and Athetosis: A Clinicopathologic Report. DR. M. NEUSTAEDTER.

Clinicopathologic reports of 2 cases are given. The first was a typical case of choreoathetosis involving the muscles of the face, both upper extremities and, to a certain extent, the lower extremities of a woman 38 years of age. The condition was supposed to have been present since birth. The Putnam operation was performed on the right side, with slight amelioration of the symptoms, and six months later on the left side. Four days after the operation infection of the wound and pulmonary edema with consolidation developed, and the patient died.

The second was a case of double athetosis involving muscles of the face, neck and upper and lower extremities of a man of very low intelligence, who was admitted to the hospital in 1918, at the age of 55 and died at the age of 73. In this case there were contractures of the fingers of the right hand and of the muscles of both hip and knee joints. There were kyphoscoliosis and considerable atrophy of the muscles of the left lower extremity.

The most destructive changes in both cases, in order of their severity, were in the neostriatum, the red nucleus, the dentate nucleus of the cerebellum and, to some extent, in the molecular layer of the cerebellar cortex, as well as in adjacent areas of the white substance and the olivary bodies in case 1. While in the case of athetosis only the large cells in the neostriatum were destroyed, in the case of choreoathetosis both the small and the large cells suffered considerable destructive change. In both cases the white substance of the brain in all areas was free from alterations. The cortex in the first case was fairly normal in cell content and architecture, but in the second it showed changes in the small ganglion cells, and while the large and small pyramidal cells appeared normal numerically they exhibited pathologic alterations. It is impossible to incriminate any particular area of the extrapyramidal system; yet it is noteworthy that in the case of athetosis only the large cells of the neostriatum were involved, while in the case of choreoathetosis both the large and the small cells were affected. In cases of chorea recorded in the literature, as well as in my previously reported cases, only the small cells of the striatum had undergone destructive changes. It seems to me that the neostriatum bears the brunt of the disease and, I dare say, is primarily and mainly responsible for the symptoms.

DISCUSSION

DR. TRACY J. PUTNAM: There are one or two questions which I should like to ask Dr. Neustaedter. One concerns the differentiation of athetosis and choreoathetosis. I must admit that after a considerable acquaintance with this group of syndromes I find it very difficult to know where one category begins and the other ends. It is customary to divide the cases into those of dystonia, athetosis, ballism, chorea, and so on, but I notice that some of my colleagues will call the disease in a given case chorea while another group will call it athetosis and still a third will think it falls into the dystonia group. I find it very difficult, therefore, to

be certain that these conditions represent entities, and not variations of a single very large group of disorders. Of course, there are certain clinical entities that can be clearly marked off, such as Sydenham's and Huntington's chorea, but I think it was not in this sense that Dr. Neustaedter was speaking of chorea in the cases presented this evening.

I also wonder whether one is justified in the belief that the involvement of the large cells alone differs in more than degree from involvement of both the small and the large cells. In experimental lesions produced, for example, by anoxia of the cortex and of the basal ganglia it seems to be a fairly general rule that the large cells suffer most and first and that only as the damage increases in scope do the small cells also suffer; I wonder whether the difference between the 2 cases presented was not one of degree rather than an absolutely qualitative difference. That is a question which is much easier for the man who looks at the sections to decide than for the one who listens to the presentation; so I should like Dr. Neustaedter's comment on this.

I am also curious to know more about the result of the operation—whether it was strictly limited to the anterior column and spared the pyramidal tract and to what extent neighboring structures in the cord were involved.

This group of diseases is one which seems to me to deserve particularly intensive study at this time. The groundwork has been laid by the great masters of the heroic period of neuropathology, and the present generation is in a position to consolidate those gains and to draw more definite conclusions than have heretofore been possible; it is to be hoped that from the study of pathologic cases one can progress to physiologic studies on animals and patients which will illuminate the mechanical as well as the structural changes in diseases of this type.

DR. M. NEUSTAEDTER: In regard to the differentiation of choreoathetosis and athetosis, I have moving pictures of both patients whose cases were presented, the one before and after operation. The chairman suggested that I omit them because all know what these conditions are and the time is limited. I have studied the patient with choreoathetosis for a considerable period; at one time there was a question whether the condition was not simply dystonia. One of my colleagues thought it was a dystonic disturbance. There were distinct athetoid movements, for when the patient was asked to do something, or when she was only addressed, she would begin with the typical movements of athetosis, but at the same time she would have the bizarre movements of the muscles of the hands, face and neck; hence there was an element of dyskinesis. The movements were quick—much faster than those in ordinary dystonia—and besides there were the bizarre movements. The slides show involvement of both the large and the small cells of the neostriatum, which seems to me to clinch the diagnosis. The other case was one of pure, ordinary athetosis, the slow, hypokinetic movements, without the bizarre movements one ordinarily sees with the choreoathetotic syndrome.

With regard to the experimental phase, it must be borne in mind that there are different types of cells in the basal ganglia. Experimental evidence is not of particular value, for if one injures all the cells one still does not know why there is hyperkinesis in one condition and hypokinesis in the other. It is not known why there are the quick movements in dystonia, slow movements in ordinary athetosis and bizarre movements in chorea.

In the operation, only the anterior columns were sectioned. The slides show a marked defect on the right side and a lesser one on the left side. The peculiar feature is that no other structures were involved and that secondary degeneration did not follow that incision; there is no question that there was an incision, for the cord shows it to be there. Dr. Putnam sent me three slides of the cords in his cases, and in one of these I found something very similar to the particular involvement of the white matter around both anterior horns in my case. If there had been a degenerative process below the anterior horns as a result of the section, there would have been the substitution of some glia. Stains of serial sections for glia revealed nothing in this region but a space from which the fibers were gone, similar to the lesion in Dr. Putnam's cases. The process seems to be a

congenital abiotrophic one, since there was no evidence of secondary change as a result of the section. The improvement in the right side was fair, but not great. Why the patient afterward had weakness in the right upper and lower extremities I do not know. The lateral tracts were not involved at all.

Mimetic Smiledness as Related to Handedness: An Indicator of Basic Modes of Human Adaptation. Dr. John G. Lynn (by invitation).

In 1937 I conducted a preliminary study on 84 normal subjects in which the relation between the prevailing form of hand-smile laterality and certain aspects of the personality and mode of adjustment was investigated. A further study of the problem was carried out in 1938-1939 on 82 abnormal patients at the New York State Psychiatric Institute, using better controlled and more objective and quantitative statistical technics. The essential findings were similar for both groups of subjects. Well defined homolateral hand–mimetic smile dominance (right handedness with right smiledness or left handedness with left smiledness) was found to be an indicator of the so-called A mode of adaptation and adjustment, consisting of the following behavior and personality traits: initiative, self-confidence, resistance to molding, courageousness, preference for the new and unfamiliar, adventurousness, aggressiveness, independence of authority, creativeness or originality, fight reaction, dominating personality, leadership, sense of social security, individual orientation, quickness of reaction, high affectivity and emotional responsiveness. Well defined contralateral hand–mimetic smile dominance (right handedness with left smiledness or left handedness with right smiledness) was found to be an indicator of the so-called Z mode of adaptation, consisting of the following behavior and personality traits: lack of initiative, social shyness, malleability, timidity, preference for the old familiar, cautiousness, retiring disposition, dependence on authority, imitativeness, flight reaction, subservience, a follower, sense of social insecurity, conformity to convention, slowness of reaction, low affectivity and emotional responsiveness.

Correlation of homolateral and contralateral hand-smile laterality with the ratings on A and Z behavior traits in the 1937 study gives an approximate coefficient, r, of $+0.76$, with a probable error of ± 0.03, and with the ratings in the 1938-1939 study, a coefficient of $+0.60$, with a probable error of ± 0.05. The data from the two studies also indicated that the Z pattern does not attain its mature development in connection with contralaterality until after the age of 14 years, while the A pattern is well established in cases of homolaterality during childhood.

From the foregoing developmental differences, it may be inferred that the earlier developing A pattern has, in all probability, a predominant subcortical determination and that the later developing Z pattern has a predominant cortical determination. This inference from the data of the study is supported by the reported results of bilateral cortical ablations, as well as by hypothalamic stimulation in both men and animals.

But how can the occurrence of smile laterality on the same side as or on the side opposite the cortical motor handedness be neurologically connected with predominance of the subcortical A or the cortical Z mode of adjustment, respectively?

Recent evidence indicates the existence of a normal diencephalic motor laterality, manifested in parotid glandedness as well as in mimetic smiledness, which is just as empiric as, although somewhat less stable and less general than, cortical motor laterality, manifested in handedness. The character of the prevailing diencephalic-cortical interaction, and hence of the prevailing mode of behavior, may conceivably be profoundly modified by whether or not the hyperactivity of the diencephalic motor laterality is on the same side of the brain as the dominant cortical motor areas or on the opposite side.

Extreme smile laterality on the same side as the handedness would reflect a maximum diencephalic emotive activity on the same side as the dominant cortical motor patterns. In keeping with the physiologic characteristics of crossed and uncrossed reflex pathways in the spinal cord, the few-neuroned, direct, ipsilateral

diencephalic-cortical integration should transmit any diencephalic excitability to the cortex with maximum rapidity and intensity. In Pavlov's (Conditioned Reflexes and Psychiatry, translated and edited by W. Horsley Gantt, New York, International Publishing Company, 1941) and Krasnogorski's (Physiology of Cerebral Activity in Children as a New Subject of Pediatric Investigation, *Am. J. Dis. Child.* **46**:473 [Sept.] 1933) terms, this strong infracortical reenforcement of the cortical cells would cause these cells to have a maximum positive and a minimum negative conditionability. In other words, the homolateral subject's cortical cells would have a high level of stimulus tolerance, and his goal responses would exhibit a strong resistance to environmental overstimulation and disruption, manifested in the persistent satisfaction of appetites and the realization of potential capacities, with the development of mastery technics through adventuring and aggressive activities, even in the face of frustration and danger.

In the case of a child with extreme smile laterality on the side opposite his handedness one might expect that throughout development the physiologic characteristics of the crossed, many-neuroned commissural pathway between the dominant side of the diencephalon and the dominant side of the motor cortex would play a persistent role. The speed and intensity of the transmitted excitatory process would be minimal, and so the unlearned infracortical patterns would give minimum reenforcement to the learned patterns of the cortex. Such a lowering of the general level of excitability of the cortical cells, according to Pavlov, decreases their positive and increases their negative conditionability and so gives them a prevailing low level of stimulus tolerance. This could operate during the development of the contralateral subject as a relatively constant factor disposing to the growth of a Z mode of adjustment and manifested in marked vulnerability to having goal responses disrupted and negatively conditioned by actual or potential dangers and frustrations. Thus, such a subject acquires as his most natural mode of adaptation the Z pattern, based on conformity, avoidance and, finally, dependence on authority for security and for guidance and protection in obtaining at least a minimum of satisfaction of appetites and realization of capacities.

DISCUSSION

DR. CHARLES DAVISON: Dr. Lynn has utilized ingenious cinematographic methods for measuring degrees of behavior, handedness and mimetic smiledness. In this short presentation he has been able to give only a fragment of his extensive investigations. The biologic, developmental and social significance of the A and Z patterns he elaborated and their mode of adjustment will prove of significance in the understanding and treatment of some of the psychoneuroses. The observations on gestures in human beings and in animals, especially those of the hand and face, have interested a number of investigators. Darwin, although little cited on this subject, wrote an excellent treatise on emotions, based on gestures and movements. He, like Dr. Lynn, pointed out the one sidedness of smiling in some people. To a certain extent it is possible to tell what goes on in the mind of a patient by observing movements of the face, hands and other parts of the body. This is especially true of psychotic persons and patients undergoing analysis or psychotherapy who have long periods of silence.

The well defined homolateral hand–mimetic smile dominance with the majority of cases of right handedness and right smiledness and the minority of cases of left handedness and left smiledness is of interest from the neurophysiologic point of view. It is needless to repeat the connection between this phenomenon and the dominance of the speech center in the left hemisphere, which, in turn, is also in intimate relation with the person's emotional life. Emotional dominance must be influenced by that part of the cortex through which one acquires language and symbols. Every neurologist is familiar with the lability of emotional outbursts or disturbances associated with lesions of the central nervous system, especially in aphasia with a pronounced motor aspect. These aphasic patients, who know what to express but cannot do so because of the motor speech deficit, show their impatience by various gestures.

Although classifications have a definite purpose, one should also remember their limitations. I do not know whether I can go as far as Dr. Lynn and accept his classification of A and Z patterns on the basis of the mode of adaptation and adjustment and their relation to hand–mimetic smile dominance. There are so many factors in the person's development that to define types of behavior solely on the basis of hand–mimetic smile dominance appears dangerous.

I wonder whether the fact that neurotic traits are more prevalent in the Z pattern and that the Z mode of adaptation does not undergo noticeable development until after the age of 14 is not in harmony with the idea that the neuroses coming on at or near puberty are only the expression of a revival of earlier, infantile and childhood disturbances. Dr. Lynn has brought this out in his observation that neurotic traits in childhood of the Z pattern become further accentuated in adolescence.

I am not sure that negatively conditioned behavior patterns in animals are a function of the cortical inhibitory process, as postulated by Pavlov and others. Negativistic reactions in persons with tumors of the frontal or temporal lobe or other lesions have been observed by every experienced neurologist. Dr. Lynn's conclusions are acceptable if one uses the term learned adient reactions or responses. One may speculate that the earlier developing A pattern of adaptation has, in all probability, a maximum subcortical determination. The idea that the frontal and temporal lobes have the special function of regulating, inhibiting and socializing the expression and satisfaction of subcortical affection, appetites or drives appears reasonable. I do not know whether one can speak of early cortical Z patterns. It seems to me that early Z patterns are possibly also subcortical. They are little influenced by the cortex until later in life, when the cortex begins to integrate as a result of experience and learning.

It is well known that subcortical functions are released in more primitive, relatively unconditioned and less socialized forms of expressive and adaptive behavior after injury to or removal of the frontal lobe, especially when the injury or excision is bilateral. The fact that in bilateral removal, injury or tumor of the frontal or temporal lobe there is accentuation or loss of A and Z traits shows that these patterns are influenced by and are under the control of the cortex. One cannot say, therefore, that some traits are subcortical while others are cortical.

The fact that smiledness is under cortical and subcortical influence is further illustrated by the loss of mimetic innervation in cases of cortical or thalamic lesions. The cases of lesions of the temporal lobe reported by Friedman and Schick, with loss of mimetic innervation, and the cases of pathologic laughing and crying reported by Kelman and myself indicate that the cortex may be concerned with this type of function. One may cite Hughlings Jackson and Bard to the effect that decortication acts as a "release" of the subcortical rage mechanism from the inhibitory influence of the cortex.

The A and Z patterns of Dr. Lynn remind one also of the classification of patterns by Kretschmer and others. Krasnogorski's further classification of behavior in children into the subcortical, the cortical, the central well behaved and the anergic, or hypodynamanic, type seems too far-fetched. The normal child exhibits a little of every variety, while the behavior of the abnormal child or of the grown-up person may approximate a specific variety.

The whole pattern of behavior is a complex one, and it must be understood in terms of totality and not alone in terms of its relation to the chemistry of the body, the body build and glandular organization of dynamic patterns of behavior or the dynamic neural relation of handedness to involuntary smiledness. All studies of these isolated factors are of importance, but the patient's behavior should be studied or understood in terms of all the data available.

I cannot fully agree with Dr. Lynn that the late growth of the Z pattern in general is of cortical and educational determination. It seems to me that inhibition of emotional initiative, social shyness, extreme cautious foresight of physical danger and dependence on secure authority are also dependent on subcortical function, while traits of the A pattern, such as independence, self confidence and judicious

fight responses, are dependent on well integrated cortical rather than subcortical function. Because the Z pattern in general develops mostly after 14 years of age, especially the last six traits mentioned, one cannot conclude that it is under cortical influence.

I am glad that Dr. Lynn has defined the traits of the A and Z patterns in accordance with whether they are purely primitive emotional reactions or whether they are integrated emotional responses influenced by judicious cortical control. In other words, an aggressive act belonging to the A pattern, if used when indicated, may be an appropriate and justified act and well under cortical control. On the other hand, a Z trait, like flight, may conform to a reality situation, such as a real dangerous situation, and may be well planned out in advance and also under cortical control. Traits such as flight, avoidance, caution and inhibition, found in the Z pattern of reaction, should be interpreted in terms of reality or unreality. Are they acts which are justified, or is the person fleeing, avoiding or being cautious or inhibited because of unreal situations? In other words, flight, avoidance, caution and inhibition may be under either cortical or subcortical control. The decorticated human being, if I may use this term for some persons, may become extremely aggressive under the least provocation and also extremely frightened when there is no justification for such fright. In other words, the traits of A and Z patterns are relative and can be influenced by both the cortex and the subcortex. When under subcortical control, they are more likely not to conform to reality situations.

DR. WLADIMIR ELIASBERG (by invitation): The method which Dr. Lynn described may become important for a study of those mimetic and expressive processes that are dealt with in physiognomy. So far there are anatomic physiognomy, on the one hand, and psychologic physiognomy, on the other. Between the two there is a gap. To fill this, a physiologic physiognomy is needed.

About sixty years ago William James, objecting to the psychologic physiognomy, stated (Principles of Psychology, New York, H. Holt & Co., 1890, vol. 2): "My theory, on the contrary, is that the bodily changes follow directly the perception of the exciting fact and that our feelings of the same changes as they occur is the emotion. Common sense says, we lose our fortune, are sorry and weep . . . the hypothesis here to be defended says that this order of sequence is incorrect [page 449]. . . . It must be admitted that it is so far only a hypothesis and that much is lacking to its definite proof [page 454]." Indeed, if one could have a record of the exact timing of the processes, a new experimental physiognomy could be created, just as experimental psychology was the result of introducing methodical investigation of the timing of psychologic processes.

The "mickey mouse chamber" of Dr. Lynn may yield such exact time records and may become the inseminated ovum of the new physiognomy. May I express my hope that Dr. Lynn himself will direct his attention to those problems that are interesting to the psychologists?

DR. PAUL FREDERICK ADAM HOEFER: I should like to ask Dr. Lynn if he has ever studied mimetic smiledness in patients with manic-depressive psychosis, both in the manic and in the depressive phase.

DR. ABRAM BLAU: I, too, have been interested in the subject of handedness for a number of years, particularly in relation to specific reading disability and stuttering. Dr. Lynn's theory seems to be similar to that presented by Dr. Orton some years ago, in which he explained reading disability on the basis of mixed dominance.

However, as one studies these reading disabilities, one finds more and more that the disturbance is not caused by mixed dominance in all cases. There are many patients who have no history of left handedness who have been retrained to right handedness. One also meets, particularly in the school system, many patients with left handedness who have been retrained to right handedness, with no subsequent ill effects, such as stuttering or reading disability. Nevertheless, it is true that left handedness is far more frequent among stutterers and those with reading disabilities than among the general population. It has occurred to me that there

is a possibility that left handedness and the syndrome of stuttering and reading disability may be associated symptoms in one personality disorder rather than disturbances having a causal relation to each other.

On investigating the whole question of handedness, one finds it generally assumed that one is right handed because one is left brained. The question, however, can be raised: Is one left brained because one is right handed? This suggests that dominance is an acquired, rather than an inherited, characteristic. If one reviews the literature (and there is a great deal written on handedness and the whole question of dominance) one finds there is no definite proof of the hereditary nature of dominance or handedness. I personally have not had the good fortune to do the excellent statistical work which Dr. Lynn presents, but in the large number of situations in which I have had the opportunity of investigating the family history I could not find any evidence which really suggested a hereditary nature of dominance or handedness. Another point is that anthropologic studies of handedness tend to show that primitive man was not right handed or definitely left handed. As a matter of fact, studies of primitive writings, pictures and implements show that until the Bronze Age, when specific instruments were invented, definite handedness was not established, and there seemed to be as many left-handed as right-handed persons. In various cultures there is also a difference in handedness. I should like to ask Dr. Lynn whether he feels that handedness is a definite hereditary characteristic and whether he has not considered the possibility that handedness itself may be a neurotic manifestation from early childhood. Left handedness would thus show failure in social adaptation, since the child lives in a culture which tends to influence him to accept right handedness. The child who does not accept right handedness is, in a sense, antagonistic and negativistic to the accepted cultural trend.

DR. SAMUEL T. ORTON: I have nothing of real significance to add to this discussion. I have been intimately studying the question of handedness in cases of stuttering and reading disability for fifteen years, and I have seen a very large series of cases of reading disability and of other conditions which I think have their neurologic basis, or stem, in confusion in cerebral dominance. I have no actual statistical figures, but I myself am thoroughly convinced that left handedness is transmitted as a hereditary pattern. As a matter of fact, the distribution figures for right handedness and left handedness in the general population would bear this out strongly, in a ratio of about 9:1, which is what one would expect in a recessive character.

One probably makes a mistake in attempting to associate too closely conditions like reading disability with the handedness pattern. The great majority of my patients with reading disability are right handed. Many of them are also right eyed and right footed; in other words, many of them have distinctly unilateral motor patterns, but this does not preclude the possibility of a confusion of dominance in the parts of the cortex which have to do with the reading process, and one sees the same symptoms as in those who do have confusion in the motor patterns.

DR. JOHN G. LYNN: With reference to Dr. Davison's main comment, namely, whether it is valid to associate the Z pattern of traits with the cortex and the A pattern with the subcortex in quite as strong a manner as I have apparently impressed him as doing, I should like to make one point. I did use one word with a great deal of caution. I spoke of *predominant* cortical and *predominant* subcortical dominance with the idea that there is no such thing as *total* cortical or subcortical dominance. The data show that there are certain traits in the Z pattern, for example, preference for the old and familiar subservience, flight reaction and timidity, which are developed much more in childhood than they are in adulthood. However, the majority of the Z traits, especially those like caution, which implies thinking in terms of past experience and possible dangerous consequences, or dependence on authority, which implies having some experience with authority, are developed to the greatest extent after the age of 14. Those traits of the Z pattern that develop before the age of 14 seem to be the more primitive

ones and express a certain vulnerability to disruption of goal responses, which later on makes the person more dependent and more cautious. The A pattern also shows certain traits which do not develop to a maximum degree in childhood but do develop more after the age of 14, but there are only two of these, namely, leadership and socialized aggressiveness. One might expect that primitive, child-like dominance and unsocialized aggressiveness, when socialized, might develop into effective leadership. The socializing factor seems to be important and is presumably tied up with cortical functions, even in the A pattern, although the majority of the traits in this pattern show predominant development before the age of 14.

I appreciate the comments of Dr. Eliasberg on the use of the apparatus. I hope to improve on it. My associates and I are trying to work out a way of obtaining electromyographic records of action currents of the facial muscles so that we can get a continuous action record along with the photographic records.

Dr. Hoefer raised an interesting question about the changes in laterality of the face in connection with manic-depressive episodes. I have the records of 6 patients with what was diagnosed as manic-depressive psychosis who have shown, along with changes from the manic to the depressed phase, clearcut shifts in facial laterality, as observed by myself and several other physicians. Unfortunately, I have not had the proper equipment for photographing these shifts. Recently, there have been 2 patients at the Long Island Home who have had most dramatic shifts of facial expression as they changed from the depressive to the excited phase. It might seem, on the basis of these 2 cases and the 4 cases which I have observed at the McLean Hospital in Waverly, Mass., that these shifts in laterality might offer a means of fuller understanding of some of the dramatic personality changes associated with manic-depressive psychoses.

Dr. Blau, I believe, has asked me to comment on the hereditary determination of handedness. I am afraid I cannot do this because I have not had enough experience with it. I know that work has been done, but I do not feel in a position to comment with any authority on the matter. All I did was to measure handedness by tests which are standardized and recognized as reliable.

I appreciate Dr. Orton's comments on his work, because I think that I have studied a form of laterality on which heretofore he has made no observations. I might suggest that while his pathologic deviations with reading disabilities and stuttering seem to be connected with a mixed or equivocal dominance on the same cortical level, here another form of lateral dominance is involved, namely, emotional smiledness, occurring on the same side as the handedness or on the opposite side, but at a different level of the nervous system. Whether this is connected with stuttering or reading disabilities I do not know.

Marginal Dyskinesias and Dyssynergias: Diagnostic Adjuncts. Dr. Byron Stookey and Dr. Lester Mount (by invitation).

Frequently patients are seen who show signs of an expanding mass without sufficient evidence to warrant localization. In many instances it is difficult to determine whether the lesion involves the left or the right cerebral hemisphere. In investigating this problem, it was found that in some patients the gait as usually tested was entirely normal or showed only slight abnormalities whereas quadrupedal gait, with the subject either on the hands and knees or on the hands and toes, frequently demonstrated abnormalities not previously evident or accentuated abnormalities already noted.

In the upper extremities, these abnormalities consisted of diminished flexion at the elbow and at the wrist or an abnormal attitude of the extremity as a whole. The extremity was advanced in a stiff manner or might allow but little weight to be supported by it.

In the lower extremities, a shorter pace on the involved side, dragging of the foot or knee, circumduction of the lower extremity, inversion of the foot, diminished flexion at the knee, advancement of the lower extremity in a stiff manner, or

carrying of the leg so as to bear but little of the body weight was noted. Frequently the pelvis tilted toward the affected side or was thrust to the opposite side.

An attempt was made to show that the neurologic examination should not be considered complete unless the dyskinesias and dyssynergias brought out by quadrupedal gait are tested. It is felt that these tests are of distinct help in the neurologic examination.

DISCUSSION

DR. ISRAEL S. WECHSLER: The demonstration of the quadrupedal gait brings to mind a few physiologic facts which may be of interest in connection with the anatomic localization to which Dr. Stookey alluded. Obviously, there is dissolution of upright posture when the human being walks on all fours. Several years ago Russell Brain described the quadrupedal extensor reflex, which consists of the extension of the flexed hemiplegic arm when the patient walks on his hands and feet. He also observed that in the quadrupedal gait the arm is more extended if the head is bent back and flexed if the head is bent forward. Obviously, the maneuver influences both tonus and posture and may be correlated with the tonic neck reflexes described by Magnus. As a matter of fact, one can demonstrate in some cases of hemiplegia the presence of tonic neck reflexes, that is, increase of the spasticity or the extension of the paretic limb if the chin is turned to the hemiplegic side and loss of tonus or flexion if the occiput is rotated to that side. I noticed that practically all of the patients presented by Dr. Stookey held their heads rather high in order to see better, but the extension of the head increased tonus and affected posture at the same time. Also, when the patients lay on the table with the head extended beyond the edge the tonus in the paretic arm seemed to be increased. While one does not expect to elicit tonic neck reflexes in cases of cerebellar disease, changes in tonus and posture may be associated with such lesions. Generally it is a question of decortication and decerebration, and the presence of *Stellreflexe* (postural reflexes) and tonic neck reflexes points to localization all the way from the cortex to the midbrain and upper portion of the pons. It may be that what Dr. Stookey has shown will throw light on the physiology of quadrupedal gait and its relation to anatomic localization.

CHICAGO NEUROLOGICAL SOCIETY

ROY R. GRINKER, M.D., *President, in the Chair*

Regular Meeting, Nov. 27, 1941

Paraplegia Following Use of Abdominal Tourniquet for Postpartum Hemorrhage: Report of a Case. DR. NORMAN A. LEVY and (by invitation) DR. HERMAN STRAUSS.

This paper will appear, with discussion, in a future issue of the ARCHIVES.

Intramedullary Trigeminal Tractotomy: Report of Twenty-Five Cases. DR. LAWRENCE WEINBERGER.

This article will appear in a future issue of the ARCHIVES.

Therapy of the Neurogenic Bladder. DR. HAROLD C. VORIS and (by invitation) DR. HERBERT LANDES.

The rational treatment of the neurogenic bladder has been neglected in the past; yet there is no other factor so essential to the health or comfort of the patient with this condition.

Cystometric studies are of great value in the diagnosis and management of the neurogenic bladder, but if a cystometer is not available, careful clinical obser-

vation plus the use of the catheter to determine the presence of residual urine will enable the physician to manage these patients adequately.

After an acute transverse lesion of the spinal cord or cauda equina the bladder is not completely atonic, but a considerable pressure develops during filling. Such bladders should be drained with the indwelling urethral or suprapubic catheter.

In the atonic bladder of tabes dorsalis little or no intravesical pressure develops, and consequently constant drainage is not necessary unless the bladder contents are infected.

The bladder that is uninhibited and empties itself precipitantly does not require constant drainage except to keep the patient dry, and this can be accomplished usually with some form of urinal. Suprapubic drainage is never indicated in cases of this condition, as the patient will void intermittently through the urethra in spite of the presence of the suprapubic catheter.

DISCUSSION

DR. NORMAN A. LEVY: I should like to ask what experience the authors have had with mecholyl (acetylbetamethylcholine).

DR. PERCIVAL BAILEY: The authors did not mention sympathectomy in the treatment of cord bladder. I should like to know whether they abandoned this procedure because they found it ineffective.

DR. HAROLD C. VORIS: What little experience we have had with mecholyl has been disappointing. In a few cases there has been some immediate improvement, but in no instance have such results been retained.

The classification I made was for the purpose of discussion rather than from any conviction on my part that a rigid classification was possible. When injury to both motor and sensory components of bladder innervation are present, cystometrograms are of value, and the method of management should depend on whether the patient exhibits any bladder contraction with filling and whether he is able to supplement bladder contractions with physical means, such as suprapublic pressure or abdominal straining.

We have not felt that presacral neurectomy has sufficient effect on the motor function of the bladder to warrant its use in cases of urinary retention—so-called cord bladder.

NEW YORK NEUROLOGICAL SOCIETY

ABRAHAM A. BRILL, M.D., *President, Presiding*

Regular Meeting, Dec. 2, 1941

Ophthalmologic Aids in Neurologic Diagnosis. DR. ISADORE GIVNER (by invitation).

When one considers that six of the cranial nerves have representation in the eye and its appendages it becomes apparent why intracranial lesions are frequently recognized first by the ophthalmologist. In more recent years the field changes associated with opticochiasmal arachnoiditis of syphilitic origin have led to diagnosis and subsequent operative intervention, with resulting improvement of vision in about 20 per cent of cases. It is with the idea of calling attention to four less spoken-of syndromes that this presentation is made.

1. Association of sclerosis of the cerebral basal vessels with optic nerve atrophy and cupping of the optic disks.

2. Retinal changes in tuberous sclerosis. Observations were made on a 5 month old infant, the youngest patient to be reported on while still alive. General examination showed nothing to account for convulsions until a study of the fundi was made. The appearance both of the retina and of the optic disks has changed

during two years of observation in that a new lesion has appeared in one eye and the associated edema in the opposite disk has extended to involve the macula, giving a cherry red spot. An encephalogram taken after examination of the fundi showed the typical "candle droppings" of the ventricle.

3. Ocular changes in the postencephalitic parkinsonian syndrome, as observed in 17 consecutive cases. The following signs were emphasized: (*a*) Inability to use the accessory elevator (frontalis) muscle, varying in degree from complete inability to noticeable diminution in function. However, this muscle was brought actively into play at the time the eyes rolled up to fix. (*b*) Oculogyric crises. The influence of premotor cortical excision as performed by Klemme was observed. (*c*) Cogwheel movements of the eyes on looking from side to side. (*d*) Convergence insufficiency.

4. Cyclic oculomotor paralysis, as observed in the 32 reported cases. In the case described the phenomena consisted of complete paralysis of the third nerve on the left side. The patient had ptosis and enlargement of the pupil on the left side; the pupil measured 8 mm. and reacted only sluggishly to light and consensually. After observation for one minute a little twitching arose in the upper lid, and gradually this became quicker and livelier, ending with complete opening of the palpebral fissure. At this moment the pupil contracted to 3 mm., while the normal, right pupil kept its usual size. After twenty seconds the left upper lid fell slowly, and at the same time the pupil again dilated. This cycle repeated itself at irregular intervals all day long. It occurred once or more during sleep, awakening the patient. During the spastic phase refraction showed an increase in myopia, of 2 D., indicating the association of the ciliary muscle in the spasm. Pupillographic examination by Dr. Otto Löwenstein gave the following responses:

(1) The right pupil dilated slightly when the spastic phase involved the left eye. (2) Five seconds was required for the pupillary contraction in the spastic phase to reach its greatest intensity and nine seconds for the subsequent maximum dilatation. (3) The left pupil reacted to near point fixation to the extent of 0.3 mm. but did not react consensually until the diameter was 6 mm. or over.

Oculomotor paralysis did not develop until the patient was 22 years old, a few months after resection of the levator muscle for the congenital ptosis which was a part of the complete paralysis of the nerve.

I wish to emphasize that in the interpretation of observations and suggestive aids to diagnosis the close interrelation of neurology and ophthalmology is apparent.

DISCUSSION

DR. GEORGE A. BLAKESLEE: Dr. Givner has brought to attention the frequency with which ocular signs are recognized by the ophthalmologist in cases of organic disease of the central nervous system and of diseases within the calvarium, with resultant involvement of the cranial nerves. His paper deals with the ocular signs associated with the following less common conditions of the nervous system.

Sclerosis or Calcification of the Cerebral Basal Vessels.—The changes in the visual fields are not uniform but are dependent on the portion of the visual apparatus involved. The internal carotid arteries are probably most commonly affected, but in a case at the New York Post-Graduate Hospital in which I was interested a diagnosis of neoplasm of the pituitary was confirmed by operation, the tumor elevating the optic chiasm so that it lay against the anterior cerebral artery, with actual notching of the right optic tract. Examination showed changes in the left homonymous quadrantic field. The differentiation between glaucoma with changes in the fundus and visual field and other conditions, such as sclerosis or calcification of basal arteries, may be difficult, but is extremely important. It seems to me that the most important observation in this case was the normal or only slightly elevated intraocular tension associated with the ocular signs due to vascular disease, while in glaucoma the intraocular tension is increased generally without great variability in the tension. The field changes, also, are usually more altitudinal in vascular disease and are not of progressive character, as in glaucoma.

Tuberous Sclerosis.—With this rare congenital disease, which affects chiefly the cerebrum, there are associated adenoma sebaceum and tumors elsewhere in the body, together with epilepsy and mental deficiency.

Cases have been described in which tumors were present in the retina without accompanying changes. Van der Hoeve discovered such a retinal tumor, but its real nature was revealed when investigation of the family laid bare the fact that five brothers and sisters were suffering from advanced tuberous sclerosis. Without the family history the diagnosis would undoubtedly be difficult, for either the ophthalmologist or the neurologist.

Postencephalitic Parkinsonian Syndrome.—The ocular signs described by Dr. Givner are not uncommon in epidemic encephalitis, but in my experience they are seen less frequently now than when this disease was first studied, in 1918. The oculogyric crises are not observed as often as other ocular manifestations. Frequently the crisis lasts much longer than a few minutes, and may continue for hours. The cause of the crisis, which is often of sudden onset and associated with cephalogyric movements, is not positively known, but it seems to me that the corticonuclear portion of the pyramidal tract with the aberrant fibers of the pes, both superficial and deep, may enter into the mechanism.

Cyclic Oculomotor Paralysis.—I have never seen this rare condition, only 32 cases of which have been reported, nor have I been able to find a pathologic study in any of the cases. Bielschowsky observed 10 of the cases. Dr. James W. White, director of ophthalmology at the New York Post-Graduate Hospital, has seen 1 case, that of a Negro child whom he examined and whose condition he diagnosed as complete unilateral paralysis of the oculomotor nerve. At intervals of a few minutes the upper lid was partially elevated, with a miotic phase of the pupil and associated external movement of the eyeball. I wonder whether prostigmine might aid in relieving this condition, as it does in cases of myasthenia gravis.

Dr. Givner's paper has brought to our attention the less common syndromes with ocular signs; it should impress us with the importance of continued study of the anatomy and function of the nervous system.

Dr. Thomas H. Johnson (by invitation): Dr. Givner and Dr. Blakeslee have so thoroughly covered the subjects under discussion that there is little I can add.

In cases of sclerosis of the basal arteries of the brain two types of abnormal visual fields may be seen. The first are the binasal and altitudinal hemianopias. These are not common field changes. For a binasal defect to develop it is necessary that the lateral fibers of the visual pathways be involved. The most common cause of binasal hemianopia is sclerosis of the internal carotid arteries, which lie in close relation to the lateral surfaces of the chiasm. It is conceivable that binasal hemianopia might be caused by a bilateral lesion in the occipital lobe or in any part of the visual pathways in which the lateral fibers are involved. The internal carotid artery gives off, soon after its emergence from the cavernous sinus, the anterior cerebral artery, which passes forward and over the optic nerve and is in close relation to its superior surface. Pressure of a sclerosed anterior cerebral artery on the upper fibers of the optic nerve may cause lower altitudinal hemianopia. Also, the ophthalmic artery after its origin passes forward along the lateral surface of the optic nerve into the orbit, where it crosses the nerve, with resultant altitudinal hemianopia. The second type of visual field defect is the irregular, asymmetric one, due to interference with the nutrition of the optic nerves and probably also to pressure from the sclerosed basal arteries. In the cases that Dr. Knapp described (Knapp, A.: *Tr. Am. Ophth. Soc.* **25**:343, 1932; **37**:300, 1939), it seems to be, judging from the changes in the visual fields, that atrophy of the optic nerves is not due to pressure from sclerosed vessels so much as it is the result of changes in the vessels that supply nutrition to the nerve. Traction on the optic nerve may cause defects in the visual fields. Cushing stressed the importance of traction on the chiasm in its effect on the visual fields in cases of pituitary tumor. A lesion that lifts up the optic nerve and causes it to impinge on the optic foramen can cause field changes by destruction of the fibers in the

superior portion of the nerve. Or depression of the nerve may cause destruction of the inferior fibers by pressure against the inferior rim of the optic foramen.

I suggest caution in interpreting visual field defects, as the seemingly characteristic bilateral altitudinal hemianopia may be caused by a tumor of the frontal lobe. I have seen 2 such cases.

In glaucoma an increase in the intraocular tension is a distinguishing feature. There are cases of glaucoma with changes in the visual fields and the optic nerves in which an increase in the intraocular tension is not observed at routine and frequent examinations. It is often necessary to hospitalize the patient and have the intraocular tension taken every two hours for twenty-four hour periods with a view to ruling out intermittent rises of pressure, particularly during the night.

I have under observation an interesting patient, a nurse, whose condition about twenty-five years ago Dr. Shine diagnosed as glaucoma because of cupping of both optic disks. After she came under my observation periodic examinations failed to elicit any rise in the intraocular tension, and I was inclined to the belief that her case was similar to those described by Dr. Knapp; finally, however, high tension developed in each eye, and eventually one eye had to be subjected to a trephine operation to control the tension. The tension in the other eye has been controlled by miotic drugs. Notwithstanding treatment, there has been considerable progressive contraction of the visual field of each eye. In glaucoma, as a rule, the first change in the visual field is enlargement of the blindspot, and if the disease is not controlled, a scotoma spreads from the blindspot and progressive contraction of the peripheral field continues until there is complete loss of vision.

In a condition known as drusen of the optic disk, deposits appear in the nerve head similar to those noted in the retina in cases of tuberous sclerosis. This condition has been mistaken for papilledema. I have had under observation for several years a patient with such a lesion who was sent to the neurologic department of Vanderbilt Clinic with a diagnosis of choked disk. There has been no change in her condition. The tapioca-like deposits on the nerve head readily distinguish this anomaly and should offer no difficulty to one who has had considerable experience in examination of the fundus. Dr. Algernon B. Reese has recently stressed the importance of a thorough study of cases of drusen of the optic nerve head with a view to eliminating the presence of tuberous sclerosis.

Dr. Alfred Kestenbaum (by invitation): The paper by Dr. Givner was interesting to all who have an interest in neuro-ophthalmology. It is an old experience that in different epidemics of encephalitis the ocular symptoms differ. When the first epidemic of encephalitis began, in 1918-1919, paresis of accommodation was in the foreground. In that time I observed and presented a series of cases of this type. In the later epidemics we never saw accommodation paresis in cases of encephalitis. Instead, convergence paresis became an increasingly frequent and characteristic sign in cases of epidemic encephalitis. In another epidemic such oculogyric crises as Dr. Givner found in a number of cases were frequent. I should like to ask Dr. Givner whether in his cases the oculogyric movements occurred in a precisely upward or downward direction, or in a more oblique direction, upward to the right or to the left, as we had always seen it.

I should like to add several words about the cogwheel phenomenon Dr. Givner mentioned. This phenomenon may be described as follows: The eyes can follow an object not in a steady, slow way, as they do normally, but only in a series of little jerks, which succeed one another. Several years ago we made a study of the development of the associated eye movements of infants. We found that infants in the first three or four months of life were not able to follow with a steady movement an object which excited their attention; instead, they showed such cogwheel movements. It was not before the fourth or fifth month of life that these jerks gradually disappeared and were replaced by the usual steady, slow following movement. In cases of encephalitis there seems to be a kind of return to the primitive, immature mechanism which is normal in the young infant.

The diagnostic importance of the cogwheel phenomenon may be a double one. If this phenomenon takes place to both sides, to the right and to the left, it may

be a sign of involvement of the pons and is observed especially in cases of encephalitis. If, however, the jerks take place only to one side and the eyes follow the object to the other side in a normal, steady way the phenomenon has another important significance. If, for example, the movement of the eyes to the right side is normal but the eyes follow an object to the left side in a series of jerks, the presence of a focus in the left optic radiation, in the parietotemporal medullary substance of the left side, is proved. This sign is almost always associated with right homonymous hemianopia. It should be emphasized that the occurrence of the cogwheel phenomenon to the left side (associated with right hemianopia) is caused by a focus in the left hemisphere; the movements are directed therefore to the side of the focus.

DR. ISADORE GIVNER: In answer to Dr. Kestenbaum, in the cases of the postencephalitic parkinsonian syndrome the movement of the eyes in the oculogyric crisis was straight up. The cogwheel jerks were made in both directions.

"Sham Rage" in Man: Report of Cases. DR. HERMAN WORTIS and DR. WILLIAM S. MAURER, Cincinnati (by invitation).

The available evidence leaves little doubt that the integration of the processes concerned in the emotional expressions of rage and fear occurs centrally in the hypothalamus. Here are contained the nuclei and fiber tracts which mediate the hormonal changes and sympathetic and skeletal motor manifestations commonly seen in affective states. Nevertheless, the evidence presented in the literature does not decide whether direct stimulation of the hypothalamus or absence of inhibition of its activity gives rise to the actual experience of fear, rage or other affect as such in the human being.

We therefore feel justified in presenting 2 cases of "sham rage" in human beings in the hope that they will contribute in some small measure to a better understanding of some of these problems.

REPORT OF CASES

CASE 1.—A 32 year old woman showed a decorticate sham rage syndrome after an overdose of insulin. She presented a bizarre picture: vocalization consisted of one or two meaningless words buried in a stream of unintelligible jabber. Otherwise she gave practically no evidence of any contact with her environment and would frequently assume catatonic postures. When stimulated painfully or by loud sounds or, more usually, when there was no external stimulation, she showed signs of diffuse sympathetic discharge. The reaction was stereotyped and lasted from thirty seconds to two minutes. During these attacks the palpebral fissures widened, exophthalmos occurred and the pupils dilated so widely that the iris was no longer visible. The pulse rate rose from 100 to 140 per minute and the blood pressure from 120 to 170 mm.; she would strike out blindly frequently, but by no means invariably, in the direction of the stimulation and would literally snarl and spit. The respirations were forced and rapid, and sweating was generalized. These responses were at no time purposeful. She never made any attempt to avoid the stimulus, and there was never any evidence of aggression directed against the examiners.

These reactions were observed in almost unchanged fashion for thirty days, occurring on the average of one hundred times a day. During the latter part of her stay in the hospital, and coincident with slight but definite clinical improvement, she showed much more appropriate responses. She would swear at the examiners and frequently attempt to free herself from her restraints and was seriously annoyed at the approach of the examiners. Even at this time, however, her responses were out of all proportion to the applied stimulus, and attacks continued to occur without any obvious external stimulation.

She was then sent to a state hospital, where she eventually died of pneumonia. Autopsy revealed, in addition, evidence of generalized "cerebral softening." Histologic sections, unfortunately, were not made, and no further pathologic data were available.

CASE 2.—A 24 year old white woman exhibited reactions after exposure to illuminating gas similar to those in case 1. Necropsy revealed gross congestion and hemorrhage of the cortex and subcortical white matter and anemic necrosis of the globus pallidus. There were no obvious gross or microscopic changes in the cerebellum and medulla other than hemorrhage.

Masserman, in a stimulating article, has questioned the thesis that the hypothalamus represents a center of emotional feeling. These cases, we believe, tend to confirm his point of view.

1. At no time was there any after-discharge such as would occur if the patient was experiencing true rage or fear.

2. Despite the fact that we induced several hundred "attacks," our approach to the bedside was never a source of anxiety to either patient.

3. The rage was never purposeful. At no time did either patient attempt to untie her restraints, strike the examiner or escape painful stimulation. It is, therefore, of great importance to note in case 1 that as the patient improved (and presumably acquired some cortical control) her behavior became slightly more adaptive and purposeful.

DISCUSSION

DR. E. D. FRIEDMAN: I am in accord with the authors on the interpretation of the response which they call "sham rage" as a release phenomenon, for in clinical neurology one is familiar with other forms of release phenomena. All recall the abnormal movements which occur in the wake of epidemic encephalitis, for example, the periodic fishlike opening of the mouth or the rhythmic protrusion of the tongue —expressions of release of primitive motor patterns. There is also the similar, speculative suggestion by Wilson, who interpreted the emotional disturbance of the hysterical patient as a phylogenetic recession to the level of the basal ganglia and thalamus. The patient becomes the creature of his or her emotional life in the sense of the expression of pleasure or pain, as suggested by Head. There is therefore justification for the interpretation of this manifestation as a release phenomenon, as a result of interference with the corticohypothalamic pathways and the uninhibited discharge of the hypothalamus.

I do not altogether see eye to eye with the authors on the term "sham rage." In the course of the paper they admitted they did not know whether these patients underwent any psychic processes, even though when they were approached there was no visible reaction to the presence of the examiners. It is known that a patient with the catatonic form of dementia praecox has much psychic activity going on beneath the surface, even though there is no visible expression of it and that the patient with psychopathic inferiority behaves as though he had no affect but is not devoid of affect. I should, therefore, be inclined to question the term "sham rage." I do not think one can altogether eliminate the possibility of affective experiences going on in these persons whom Dr. Wortis and Dr. Maurer have described.

This brings up the whole question that was ventilated many years ago in connection with the James-Lange theory of the emotions: Does the expression of the emotion induce the emotion—which this theory taught—or does the emotion induce the expression of the emotion? It is more probable that the expression of the emotion and the emotion eliciting it constitute a functional unit. In the one case the emotion, and in the other the expression of the emotion, is the dominant factor.

In lower animals this hypothalamic discharge is probably a conditioned reflex, but one has no right to assume that in man it is also purely a conditioned reflex, for with the progressive encephalization of function in man there must be a compounding of all reactions with psychic elements. Some may recall the cases described by Foerster, cases of tumor of the third ventricle, in which by stimulation of the floor of the third ventricle he was able to induce hypomanic and rage-like discharges. All are also familiar with the fact that even for the layman showing one's teeth is an expression of an aggressive or sadistic trend; the expression of emotion, I believe, is indicative of a compounding of the emotion with both physical and psychic factors.

I agree with the authors that the hypothalamus is not the emotional center of the body, but it is the center which controls the efferent discharges arising as a result of emotion. This paper deserves a great deal of thought and much more discussion than can be given it at this time, but I should say in conclusion that it illustrates an important new technic in the approach to neuropsychiatry, namely, the attempt to correlate physiologic, psychiatric and so-called organic phenomena in clinical medicine, a wholesome point of view in the union of soma and psyche.

DR. HAROLD E. HIMWICH (by invitation): The authors have reported the histories of 2 patients who exhibited similar symptoms acquired in different ways. The condition of one was caused by prolonged insulin hypoglycemia and that of the other by anoxia, a result of carbon monoxide poisoning. Both patients exhibited destructive changes of the cerebral cortex. The cases undoubtedly deserve much discussion because of their important implications, but in the short time allotted one can elaborate on only two or three of the points the authors have presented.

The reason for the occurrence of the lesions in the cortex of both patients should be considered. This localization probably depends on different rates of metabolism in the various parts of the brain. For example, studies of the metabolism of excised cerebral tissues have disclosed increasing rates of metabolism as the neuraxis is ascended. In the medulla oblongata metabolism is relatively low; the midbrain exhibits a higher rate, and the thalamus has a still higher one. In dogs the cerebellum and cortex come next, and the caudate nucleus has the highest rate. In man probably the cortex and the cerebellum possess the highest metabolic rates. With depression of metabolism the area with the highest rate suffers first. For that reason the cortex bears the brunt of the effects of any depression of brain metabolism.

The next point of discussion is the reason for the similar effects of hypoglycemia and anoxia. The authors mentioned that both sugar and oxygen are necessary to support cerebral functions. The lack of either sugar or oxygen will produce the same effect: depression of brain metabolism. Because the metabolic depression is common both to hypoglycemia and to anoxia, their associated symptoms and pathologic changes are similar.

With depression of brain metabolism functional ablation of the cortex ensues. This creates the experimental conditions for a study of cortical activities. One recalls the early suggestion of Hughlings Jackson that the primitive reactions of the older parts of the brain are prevented from dominating behavior by inhibiting influences emanating from higher levels. This conception is supported by studies of the symptoms occurring in cases of insulin hypoglycemia. First, cortical function disappears, perception becomes poor, speech is slurred and, finally, there is complete loss of contact. During this time the subcortical expressions of cerebral activity become evident. In therapeutic hypoglycemia these changes are reversed by the administration of carbohydrate. After brief periods of anoxia the symptoms are also temporary and cerebral functions are restored by breathing oxygen.

In the 2 cases discussed there was no return to normal. The depression of metabolism had lasted so long that destructive cerebral changes developed and normal metabolism could not be reestablished (Himwich, H. E.; Bowman, K. M., and Fazekas, J. F.: Prolonged Coma and Cerebral Metabolism, ARCH. NEUROL. & PSYCHIAT. **44**:1098 [Nov.] 1940). First, permanent loss of cerebral function was observed. The 2 patients were unaware of their surroundings. Furthermore, there was loss of the cortical inhibition usually exerted on cortical functions. This produced the phenomena of "sham rage." The dominant human pattern was replaced by another of more primitive organization.

DR. HERMAN WORTIS: We utilized the term "sham rage" because it seemed to us that these persons were not truly experiencing rage. Had they experienced rage, their behavior would have been different. To repeat:

1. At no time was there any after-discharge. 2. Despite the fact that we induced many hundred attacks, our approach to the bedside was never a source of anxiety to the patients. 3. The rage was never purposeful—in case 1 it became more purposeful only after there was a return of some cortical functioning.

In cases of catatonic dementia praecox one is dealing with an "intact" cerebral cortex. It is therefore interesting that in case 1, in which the patient was eventually sent to a state hospital, the condition was diagnosed as catatonic dementia praecox before death. Fortunately, she received no further insulin treatment.

I am sorry that time does not permit a further discussion of the James-Lange theory. I should like, however, to mention briefly the interesting work done by Grinker and Serota (Grinker, C., and Serota, H.: *J. Neurophysiol.* **1**:573, 1938) on cortical-hypothalamic relations. We of course agree that the hypothalamus may conceivably influence cortical thinking, but one must remember that in our 2 cases we were dealing with essentially decorticate preparations. The same criticism applies to Foerster's work; he mechanically stimulated the hypothalamus in persons with an intact cortex. It is therefore of great interest that Dott reported that his patients with hypothalamic lesions (Clark, W. E. Le Gros; Beattie, J.; Riddoch, G., and Dott, N. M.: The Hypothalamus, Edinburgh, Oliver & Boyd, 1938) seemed to laugh in meaningless fashion. Nonetheless, we should of course agree with Dr. Friedman that much more work remains to be done on the relation of the cortex to the hypothalamus and the extent to which the "discharges" from lower centers may be meaningful, even in the absence of adequate cortical functioning.

DR. A. A. BRILL: I have a patient under treatment now who came to me because for the last five years he has been subject to outbursts of rage which he could not explain. Last Sunday evening he was making a welsh rarebit with his wife; she walked over to him and said, "Let me have that cheese." As she took it out of his hand, he became so furious that he broke everything on the kitchen table within his reach and then refused to talk to her until this morning. He seems to be perfectly well organically. I have had him under treatment for about two months, and this is the first attack he has had during that time. He has no idea why he got so angry, and his wife, who came with him to describe the episode, could give no reason for the outburst.

Report on Family Exhibiting Hereditary Mirror Movements and Schizophrenia. DR. BERNARD C. MEYER, Orangeburg, N. Y. (by invitation).

A family pedigree was studied in order to establish what relation, if any, existed between the presence in that family of a number of persons displaying abnormal synkinetic movements and the occurrence of several cases of schizophrenia. Genetic studies revealed that the abnormal synkinetic disorder, so-called mirror movements, occurred as a single dominant hereditary factor. Its presence was noted in four generations: in the sister, father, paternal uncle, grandfather and great grandfather of 2 schizophrenic members. The incidence in the family of schizophrenia, schizoid psychopathy and other variants was consistent with the expected findings on the basis of the modern conception of the inheritance of schizophrenia as a single recessive. So far as the occurrence of each of the two conditions, synkinesia and schizophrenia, was consistent with expectations for a dominant and a recessive genetic factor, respectively, there was no reason to postulate any connection between the two. The concurrence in the family tree was therefore regarded as purely coincidental.

Three of the persons displaying mirror movements were examined physically, and moving pictures were taken. The person with the most pronounced synkinesia displayed both synkinetic phenomena and signs of involvement of the pyramidal tract. The latter consisted in generalized hyperactivity of the deep reflexes, a bilateral Babinski sign and practically unelicitable abdominal reflexes. The mirror movements occurred in both upper and lower extremities and were more pronounced distally than proximally. All movements of one hand, for example, were accompanied by a nearly simultaneous imitation by the other hand. The greater the force employed in the active "leading" movement, the greater was the response in the mirror movement. With the more proximally located movements some force was required to elicit a contralateral mirror response, whereas in the hands

and feet practically effortless motion sufficed to elicit the synkinetic movement. Moreover, movements of the upper extremities were accompanied by associated movements in the lower extremities, usually more pronounced in the ipsilateral limit. There was, however, no Magnus and de Kleijn phenomenon. The passive movement of the hands and wrists also produced a contralateral mirror response, the appearance of which was a trifle later than that produced by active movement. A strikingly similar clinical picture obtained in another member of the family except that the pyramidal tract signs were less definite. In a third case, the mirror movements were much less prominent, no passively induced mirror movements were present nor were there any signs of involvement of the pyramidal tract.

No satisfactory explanation of mirror movements has as yet been offered. Occurring as a hereditary phenomenon, they have heretofore been described but six times in the literature. However, they have been observed with some frequency in cases of ordinary hemiplegia and postencephalitic disease, in association with congenital malformation (for example, the Klippel-Feil syndrome) and, finally, as a normal phenomenon in infants and young children.

No agreement has been reached concerning the site of origin of these movements, and nearly every region of the central nervous system has been proposed, ranging from the spinal cord to the periaqueductal area, the basal ganglia and the parietal cortex. I suggest that the appearance of abnormal synkinesia is not dependent on a single site but is an expression of a release phenomenon, the appearance of which is made possible by the defective development or interruption of long extrapyramidal descending pathways anywhere in their course, in a manner analogous to the production of the Babinski phenomenon.

This paper will be published in full in the *Journal of Nervous and Mental Disease*.

DISCUSSION

DR. HAROLD G. WOLFF: Dr. Meyer has pointed out that this phenomenon, which was illustrated by motion pictures, may appear in children, and all know it may occur in chorea, where overflow is characteristic. Also, it is common in reasonably well integrated adults. Many neurologists, when teaching, draw the cerebral hemispheres with two hands or make pictures of experimental animals showing two arms and two legs. It seems to have nothing to do with any particular equipment, and I believe any one can learn to make mirror drawings. It seems, therefore, as though mirror movement patterns were something which man carries along with him and which by the slightest effort can be put to use.

I think Dr. Meyer did well to leave the pyramidal tract out of consideration, for it is now known that the toe responses to stimulation of the sole of the foot are not purely pyramidal but have other corticospinal components. All one may say is that the cerebral cortex is involved in mirror movements and that perhaps with defects in structure or function this peculiarity may come to the surface.

I wonder if Dr. Meyer would like to say a word about the relation of mirror writing or mirror movement to so-called automatic writing, such as is sometimes seen in persons with personality disturbances. For example, a person reading a novel, with the book in the right hand, may write a communication with the left hand.

DR. GUSTAV BYCHOWSKI (by invitation): I should like to remind Dr. Meyer of the investigations which were performed perhaps fifteen or twenty years ago by Dr. Kurt Goldstein and then repeated and continued by me. Goldstein started movements which he called induced movements. Certainly, in a great number of patients with different clinical conditions, as well as in some normal persons, one is able to provoke these movements, either by active movements on the extremity or by passive movements, just as was pointed out by Dr. Meyer. Sometimes it was even possible by prolonged touching of one part of the body to provoke such strange movements. It is interesting to see that in some cases it was possible by fairly small passive movements, for instance, of one finger only, to provoke movements of different limbs, and it seems to me that all these phenomena can be grouped as a part of the reflexes which Magnus and de Kleijn termed reflexes projected

from one part of the body onto another part. Moreover, in some experiments on "thalamic" animals these investigators were able to provoke similar phenomena. If this is so, one may assume in the case which has been so beautifully studied by Dr. Meyer that this kind of induced movements reveals a falling back to a lower level of functioning of the nervous system.

I should like to ask Dr. Meyer whether he was able to observe the reflex of Rossolimo in these cases. I ask this because in a certain number of cases of schizophrenia I was able to find obvious neurologic phenomena, such as a Babinski sign in some and the reflex of Rossolimo in others. If I am not mistaken, in some cases of automatic writing there also occurred movements in the other extremities similar to those which have been so well described by Dr. Meyer.

DR. E. D. FRIEDMAN: Did Dr. Meyer at any time observe any perseveration in the speech of this patient?

DR. BERNARD C. MEYER: In regard to the question about mirror writing and the relation to psychic functions which was asked by two of the speakers, it is an interesting observation that in those cases of mirror writing which have been described (there is an excellent monograph on the subject by Macdonald Critchley [Mirror Writing, London, George Routledge & Sons, Ltd., 1928]), it is stated that when a right-handed person writes with the right hand the synkinetic writing which occurs in the left hand is from right to left, as in the case of this patient. On the other hand, when the writing is initiated in the left hand the synkinetic writing which occurs in the right hand is in the normal relation, namely, from left to right. This paradoxic observation apparently is to be explained by the dominance of the so-called opticokinetic influence; that is, the whole pattern of writing has been so firmly established in the right hand that this particular alteration occurs.

With regard to the remarks of Dr. Bychowski, I think I mentioned that no Magnus–de Kleijn phenomenon was present. Neither was the Rossolimo sign exhibited either by the patient, who, by the way, is a healthy person, both mentally and physically, or by his two psychotic children.

In regard to Dr. Friedman's question, there was no perseveration of speech or indication of any language difficulties of an aphasic character.

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

JAMES B. AYER, M.D., *Presiding*

Regular Meeting, Dec. 11, 1941

Electroencephalographic Studies on Children Presenting Behavior Disorders. DR. LAZARUS SECUNDA and DR. KNOX H. FINLEY.

In cases of children and adolescents presenting serious behavior disorders the relative importance of environmental and biologic factors should be determined, since the more capable the physician is of evaluating these factors in the individual case the more rational will be the therapeutic approach. Smith found that the development of the electrocortical activity of infants follows the course of myelination in the cerebrum. Lindsley and Smith showed that the adult pattern of electrical brain potentials is not established until late childhood or early adolescence, and we have been able to show from our own studies that there are individual variations in the age at which the adult pattern is stabilized. Studies by Gibbs and Lennox; Jasper, Solomon, and Bradley; Strauss, Rahm and Barrera, and Lindsley and Cutts indicate that in a high percentage of cases of behavior problems in children one is dealing with an abnormally functioning cerebrum.

At the Boston Psychopathic Hospital we have obtained electroencephalographic tracings on 143 children presenting behavior disorders and have compared these tracings with those obtained on 76 normal control subjects. Sixty-eight

children were sent by the courts of Greater Boston for psychiatric study, and 75 were referred by physicians at the request of their parents. Of the 143 children, 125 had a normal physical and neurologic status and no history of illness involving the central nervous system. A relation between a poorly integrated personality and a history of neurotic traits was brought out in a number of cases. Investigation of the family background revealed only 18 "normal" families, and the child's position in the sibling group did not seem to play a significant role. The problems that led to admission were stealing, sexual misbehavior, temper tantrums and chronic truancy. Only 21 of the children showed evidence of being behavior problems during hospitalization.

The electroencephalographic tracings were obtained with a Grass six channel apparatus. Hyperventilation for two minutes was carried out with all the controls and with most of the patients. The electroencephalograms were classified under three (3) types: (1) the normal, (2) the immature borderline and (3) the immature abnormal. Because of the normal immaturity of the pattern in childhood, it is impossible from present knowledge to say whether an atypical pattern at a given age represents a delay in the maturity of the pattern or whether it is secondary to some congenital or acquired injury to the brain. Of the 143 children presenting behavior disorders, 26 per cent had normal, 23 per cent borderline and 51 per cent abnormal electroencephalograms, while of the 76 controls, 68 per cent had normal, 17 per cent borderline and 15 per cent abnormal tracings. As a group, the electroencephalograms of the children with behavior disorders were more vulnerable to hyperventilation than were those of the controls.

Since in a study of juvenile delinquency the Gluecks stressed the importance of a decrease in delinquency with increased maturity, it seemed advisable to divide the children into age groups. Four groups were chosen: the 4 to 9, the 10 to 12, the 13 to 15 and the 16 to 18 year groups. (Forty-six per cent of our patients were between the ages of 13 and 15 years.) The patients with behavior disorders had a greater percentage of records in each age group than the controls. However, when one compared age group with age group, there was on the whole a progressive increase in normal records and a decrease in abnormal records with increase in age. Slow activity was the most common abnormality in these patterns. In adult life slow activity is definitely abnormal, but in childhood it is a normal finding. Therefore, when a patient presents more slow activity than is consistent with a normal record for that age range, it is our belief that this may be due to a delay in the normal development of the cerebrum or to some pathologic factor. We feel that in the electroencephalogram one has either a measure of the delayed development of the cerebrum or an indication of the presence of a pathologic factor and that it is because of these factors that the child finds it difficult to make a satisfactory adjustment, either to his environment or to the impact of puberty.

DISCUSSION

Dr. Knox H. Finley: I wish to reemphasize the need of caution in interpreting so-called abnormal patterns of behavior in children presenting problems. Some of these may be due to a mild or temporary delay in the normal maturity of the nervous system. The present limited knowledge of the neurophysiologic meaning of brain wave patterns does not permit one to differentiate between those patterns which are immature and those which are due to some congenital or acquired injury to the brain. We feel reasonably certain that if some of the children with so-called abnormal patterns could be followed for a period some of their tracings would be found to have matured to the normal pattern.

A second point which we wish to have clearly understood is the extent to which we are using the electroencephalographic technic for the study of personality disorders—in this instance, behavior disturbances. The personality is far too complex a problem to be approached satisfactorily by any one method or by a few methods of study. In the utilization of the electroencephalogram in this study, we look on it as only one of a variety of means of gaining further understanding of this intricate subject. One might look on the electroencephalographic technic as lying at one end of a scale of many methods of studying personality, it being

a procedure which measures the sum of several as yet not clearly understood neurobiologic elements. At the other end of the scale are the analytic technics, which attempt to unravel the complexity of details which are part of the personality structure. Clearly, an intelligent approach to this difficult problem is to eliminate confusion from facts in all fields of neuropsychiatric endeavor and to attempt to coordinate the facts.

DR. FREDERIC A. GIBBS: I should like to ask a question, not because I disagree in any way with the authors' conclusions but because I should like some enlightenment. Are the differences in the amount of abnormality in different age groups possibly due to failure properly to adjust standards for age? Another question which occurs to me is one that Dr. Finley considered in opening the discussion. He takes the position that one should not describe abnormalities in the electroencephalogram in clinical terms. Does not the same argument apply to calling abnormal records "immature" and normal records "mature"? Some of the records which were designated as "immature" might equally well have been called "senile."

The argument can be stated as follows: Is one not right in speaking of the same thing by several names? No single name can be perfectly descriptive of a complex phenomenon. Each name refers to a single, imperfectly discerned fact. By choosing a particular term it is possible to emphasize or delimit the aspects of the phenomenon which one believes are at that time, and for the purpose of the particular study, especially important. I hope, therefore, that Dr. Finley will cling to the term "immature" until he finds another shorthand description which better suits his purpose.

DR. ROBERT S. SCHWAB: Is there any correlation between the degree of maturity of the waves and the personality traits and intelligence quotient?

Has there been any similar study of behavior on adult groups, such as those in a reform school or in a penitentiary, to see whether these immature waves persist through later years?

DR. RANDOLPH K. BYERS: From my experience I think that the intelligence quotient would probably show little relation to the electroencephalographic tracings. One gets rather queer results in psychologic studies on these children; that is, there is failure in a great range of tests, with occasional successes. I, too, wonder whether any such relation has been studied in these children.

DR. WILLIAM G. LENNOX: I was interested in the statement that none of the siblings of these children had defects of behavior. Rosanoff has written a monograph which deals with a large group of twins, one or both of whom had a behavior disorder. The incidence of behavior disorders in the other twin was much higher for identical than for nonidentical twins. He therefore concluded that inheritance is of considerable importance in these behavior disorders. It would be interesting to know whether the relatives of the children studied by the authors have immature or abnormal electroencephalograms.

None of them had seizures. I wonder whether this was the result of selection. If not, the absence of seizures would be against the conception that seizures and behavior disorders are basically related. If Henry Maudsley were here, he would certainly speak to this point. In 1871 he wrote in his book "Body and Mind":

"In children, as in adults, a brief attack of violent mania, a genuine mania transitoria, may precede, or follow, or take the place of an epileptic fit; in the latter case being a masked epilepsy. Children of three or four years of age are sometimes seized with attacks of violent shrieking, desperate stubbornness, or furious rage, when they bite, tear, kick, and do all the destruction they can; these seizures, which are a sort of vicarious epilepsy, come on periodically, and may either pass in the course of a few months into regular epilepsy, or may alternate with it. . . ."

If I may reply to Dr. Schwab's question, a study of a prison population now being made by Drs. Gibbs, Bloomberg and Bagchi shows much abnormality of electroencephalographic records.

DR. LAZARUS SECUNDA: We did not find any correlation between the intelligence quotient and the abnormal electroencephalographic tracings in the majority of the children with behavior disorders. We were not able to follow the 17 siblings who had behavior disorders, nor of course their parents.

DR. KNOX H. FINLEY: Dr. Gibbs has raised a question with regard to our ability to judge the normality of a pattern in the various age groups. It is, perhaps, possible that in a few cases our judgment is not accurate. However, in comparing the patterns of the group as a whole with those of normal persons of similar age ranges, we feel that our judgment is fairly correct. Furthermore, our results agree with those illustrated in Dr. Gibbs's "Atlas."

Dr. Gibbs raised some doubts with regard to the use of the term "immature" in describing some of these "off color" patterns in children and adolescents. It is, of course, not a descriptive term. On the other hand, it is not a term that carries a specific clinical meaning, as do "psychomotor," "petit mal" and "grand mal." The use of clinical terms in describing brain waves is misleading in that it infers one is able to make an accurate clinical diagnosis with an electroencephalographic tracing. The term "immature" carries no such inference.

Selective Service System: Psychiatric Notes on Selectees and Their Families. DR. C. MACFIE CAMPBELL.

It seemed appropriate to Dr. Ayer that during the national emergency this society should pay continuing attention to the special needs of the civilian population and of the armed forces. At the February 1941 meeting this topic was discussed (The National Emergency and Psychiatry: Civilian and Military Demands, ARCH. NEUROL. & PSYCHIAT. **45**:897 [May] 1941), with special reference to the Selective Service System and to problems of morale. When the program for the present meeting was made up, a further discussion of the Selective Service System, its methods, its results and the possible lessons to be learned from it was proposed. In the meantime the whole situation has radically changed. The Selective Service System has been seriously modified; the country is at war. It may, however, be of some value to note the following changes in the system.

It is more important than ever that the men inducted into the Army should be well selected and that those with recognized evidences of special vulnerability should be excluded. General Pershing's cable from France in 1918 should always be kept in mind.

There were certain drawbacks in the original setup of the Selective Service System; obviously, there were a certain duplication of effort, an awkward interval between the examination by the local board and that by the induction board, an unnecessary disturbance of the rejectee's economic life and some ruffling of professional equanimity when there was difference of opinion as to individual registrants. Partly on these and partly on other grounds, which it is not necessary to specify, the original scheme has been modified; the local board physicians are now instructed only to *inspect*, and not to *examine* the registrants and to reject only those who are judged after such an inspection to be manifestly unfit for service. While the examination by the local board physician is thus reduced to a perfunctory matter, he is invited to forward whatever relevant information he may have with regard to the individual registrant.

The careful screening by the physicians of the local board has thus been seriously modified, and there is no guarantee that the facilities for neuropsychiatric screening at the induction board will be correspondingly adjusted to deal with the added demands made on them. The new arrangement seems to be a retrograde step likely to reduce the efficiency of the Army and to add avoidable financial burdens in the way of compensation to the load of the taxpayers.

The new arrangement makes it superfluous to comment on the great opportunity which the original setup of the Selective Service System offered for taking stock of the neuropsychiatric status of the community and for considering what steps would enable the general practitioner to deal helpfully with a great

number of mild nervous and mental disorders which are at present seldom recognized as such and are inadequately treated.

With regard to the morale of the Army and of the community, the situation has obviously completely changed since the declaration of war. This is no time to deal with such a broad subject, to which many organizations at present are devoting earnest attention. I might comment on one small aspect of the problem. In the settings of medical work and of industry it is recognized how great is the benefit that accrues from a sympathetic social contact and the opportunity of ventilating grievances or other preoccupations that have been bottled up. Through the cooperation of the Community Health Association it was possible to get a preliminary impression of the reaction of families to the withdrawal of selectees from their usual social group. In many cases there was a feeling of grievance or of embitterment. An individual home in such a case may be a focus of discontent which is somewhat infectious, and it would be of social value to the individual in the home, to the family group and perhaps to a wider circle to see whether the situation might not be put on a more wholesome basis. For contact with such families there are frequently various workers available—nurses, welfare workers, teachers and pastors. It might be desirable if all such contacts could be utilized for the purpose of helping to establish good personal and social equilibrium in homes where there is a disturbing focus of discontent.

DISCUSSION

DR. WILFRED BLOOMBERG: Dr. Robert W. Hyde and I have done follow-up work on the efficiency of the examinations by the induction boards. We have suggested to the president of the society that Captain Hyde, who is the army medical officer in charge of induction, and I present at the next meeting a statistical survey of some 20,000 men we have examined this past year at the induction station in Boston. I shall reserve the statistical report until then.

However, a few things are brought to mind by Dr. Campbell's discussion. In the first place, our work here, which is highly organized as psychiatric work goes, will be helpful in getting the rest of the country to be more rigid about neuropsychiatric criteria. Our figures will show that the total number of rejections by the board plus discharges from the Army after men have been inducted and have served up to six months is the same as the total number of rejections plus discharges by other boards but that our rejections are much higher and our discharges much lower. We have already demonstrated here in Boston that of the men who have been sent back from camp after induction, a number had been rejected by the psychiatrists of the induction board and then accepted by regular army officers. If we get a few more of these we shall no longer have difficulty in persuading the Army that we know something about the work that it is hiring us to do.

In regard to malingerers, Dr. Campbell failed to mention the "negative" malingerer among volunteers. Among our discharges from camps there have been 7 men with epilepsy who failed to give a history of fits when they were examined before induction. Only in the last three days we examined a man with Argyll Robertson pupils, but no other signs of syphilis. He was turned down, but came back two days later and tried to slide through again. He then admitted having congenital syphilis, for which he had been treated for twenty-one years. His Wassermann reaction was negative, and he thought he could get away with it. People like this give more trouble than malingerers.

Another point is that very early last November and December we had a much higher rate of rejection for neuropsychiatric disability because the local boards misconceived the nature of their job and were allowing and encouraging men to enlist who were notorious problems in their communities. "If they are not good for anything else, send them into the army," was the attitude, and this continued until the local boards became aware that this policy was unwise from the standpoint of the taxpayers.

DR. LAZARUS SECUNDA: At the Lovell General Hospital we made a survey of the first 100 patients admitted to the neuropsychiatric section of the hospital.

An amazingly large proportion of the men admitted were enlisted, and apparently did not get the same examination as the Selective Service men. Moreover, to bear out Dr. Bloomberg's statement about "palming off" men, some of the patients gave a history of being vagrants who had crossed the state line and had been picked up by the police and given the choice of becoming a member of a chain gang or of joining the Army. They joined the Army and could not adjust to its discipline. A long stay in the hospital was necessary before they could be released from military control.

DR. HENRY R. VIETS: Dr. Campbell has indicated two trends which I feel ought to be strenuously combated. Those who took part in World War I will remember Osler's famous letter to the American medical profession, published in *The Journal of the American Medical Association*, in which he urged this country to weed out every one who was neurotic from the men who were drafted. Those who served both here and overseas realize the justifiability of his anxiety and how important his communication was to America. Unfortunately, not enough attention was paid to this warning, and now there is appearing the same tendency to take the man with a mild psychoneurosis into the Army. This must be combated with every means available, and if the examination now given by the physicians of the draft board is made less complete than formerly it can only mean the removal of one screen that helps in keeping down the number of psychoneurotic catastrophes in the armed forces. There is needed more screening of men, rather than less.

The second trend concerns the speeding up of the rate at which men are examined by the physicians on the induction boards. This, too, should be protested against, for no individual physician is capable, in four hours, of examining more than 40 or 50 men, and it is even better if the number is limited to 25 or 30. Instead of increasing the number of men per day that any one physician must examine at the induction board, more psychiatrists should be employed if additional men are to be examined. The members of this society should support the efforts of Dr. Bloomberg, and each should take his turn in doing this work as often as possible. It is a civic duty which no physician should side step, and every physician, no matter how much engaged, should try to serve on the induction board at least one or two half-days a month.

DR. M. RALPH KAUFMAN: There is another important question. What do families of these selectees think about having the men join the Army? Conditions have not changed, and there will be hard times ahead. It seems to me that physicians, social workers and nurses have an excellent opportunity here to help morale and the families' understanding. About a month ago I heard about a situation in the Navy which was just the reverse. The candidates were volunteers. It was found that in those localities where men volunteered and were rejected the rate of enlistments fell. This seemed to work as a focus of infection. The whole problem of the relation to civilian morale of the man who is accepted and the man who is rejected is important. It seems to me that this society might work out a program in relation to that problem.

DR. C. MACFIE CAMPBELL: In answer to Dr. Bloomberg, it is important to realize the work done by the induction board; his figures will be of great interest. He is perhaps optimistic when he feels he can convince the Army of something. He correctly emphasizes the fact that the Atlantic seaboard is probably doing its selective service work very well. Dr. F. W. Parsons, of New York, tried to get psychiatrists on a reasonable number of local boards; so the work in New York is being done well. I wonder how it is being done in Oklahoma, Arkansas, Alabama, Kentucky and some other states in which fewer specialists are available. I was shocked, in talking to a man from the Middle West, by his statement of the lack of interest of many local boards in their task. I am alarmed at the possibility that in some centers the men who do what is called psychiatric work on the induction boards may be delegated by commanding officers with little sympathy for their task or insight into its importance. It is important for this society to keep in touch with what is going on and to emphasize the need of

adequate psychiatric scrutiny of selectees. Any regression in the work of the induction boards would have serious immediate military and later economic consequences.

Effect of Pregnancy on the Course of Myasthenia Gravis. DR. HENRY R. VIETS, DR. ROBERT S. SCHWAB and DR. MARY A. B. BRAZIER.

Pregnancy may, and often does, cause profound changes in patients with myasthenia gravis. The literature indicates that some patients have been entirely relieved of their symptoms during the course of the pregnancy, others have been partially relieved, particularly during the latter months, and still others have been made worse. Therapeutic abortions have often been carried out during the second trimester in an effort to relieve the symptoms. The subject, however, has not been clearly set forth, and most textbooks on obstetrics, except for one or two, do not mention the disease. No patient has been continuously observed both before and after, as well as during, the period of gestation. The most valuable cases in the literature are those reported by Goldflam, in 1902, and by Laurent, in 1931. Goldflam's patient passed through three pregnancies, with improvement during each. Laurent's patient, on the other hand, showed no change during the first pregnancy, although her symptoms of myasthenia gravis had lasted for three years, had a complete remission during the last three months of her second pregnancy and became worse during each of five succeeding pregnancies. Four of these five pregnancies resulted in miscarriage at three to six months. One terminated in a therapeutic abortion at six months. As none of the last five pregnancies, however, progressed beyond the sixth month, it is not known whether complete remission might not have taken place during the last three months, an event which occurred during the second pregnancy. As all of the reports in the literature were made before the institution of prostigmine treatment in 1935, and the marked increase in knowledge of the disease as the result of this discovery, it is perhaps unfair to compare the reports prior to 1935 with those of the present. The only case of myasthenia in a pregnant woman recorded in the literature since the beginning of prostigmine therapy is the one reported by Tabachnick, in which the patient did not improve during the pregnancy but required more prostigmine during the third trimester than during the first or second (Myasthenia Gravis, *J. A. M. A.* **110**:884 [March 19] 1938). A personal communication from Tabachnick indicated that the patient was delivered without difficulty at full term and that in the following three years her condition has been little changed.

Since 1935 8 cases of pregnancy occurring in patients with myasthenia gravis have been observed at the myasthenia gravis clinic of the Massachusetts General Hospital. One patient passed through two pregnancies. Seven of the patients showed a partial remission from the disease in the first trimester or early in the second, and 6 patients had a complete remission in the late second or the third trimester. In most instances the remission was so marked that the patient felt as well as, or even better than, when she was in normal health. One patient, however, was worse during her entire pregnancy but was delivered at full term in a normal manner. There were no deaths during the pregnancies of any of our patients, and all of the patients who were allowed to continue to full term were delivered of normal children. One patient had a therapeutic abortion in another city at the end of the second month, in spite of the fact that she was already showing signs of a good remission. A second patient had her pregnancy terminated at six months because of fear of transmitting the disease to her child.

The most complete studied case was one in which careful records of the prostigmine intake and the patient's symptoms were recorded for more than two years. During that time she became pregnant and was delivered at term of a normal baby. About a month after conception she had a mild remission of symptoms, but in the second and third months she was in a condition of mild relapse. She had to increase the daily intake of prostigmine bromide from her usual average of about 150 mg. a day, in divided doses, to nearly 300 mg. During this period,

however, she gradually reduced the prostigmine intake voluntarily, and rather abruptly, in the fourth month of pregnancy, a complete remission of symptoms took place. At the same time she reduced her prostigmine intake to zero. This remission, except for one slight relapse, lasted throughout the rest of her pregnancy and continued for four months after its termination, at which time she returned to her stabilized state of myasthenia gravis with an intake of 150 to 180 mg. of prostigmine bromide a day. In other cases the beginning of the remission occurred early in the course of the pregnancy, and in at least 1 instance the patient suspected pregnancy in the first month, even before her first period was missed, because of the decreased need for prostigmine.

A few conclusions from this preliminary report are justified:

1. Myasthenia gravis is profoundly effected by a state of pregnancy.

2. Most patients have a period of remission during the nine months of pregnancy.

3. This remission may begin as early as the first month but is almost certain to begin by the fourth to the sixth month. The last trimester of pregnancy shows complete remission in most of the cases studied.

4. Under modern conditions of diagnosis and treatment, therapeutic abortion appears not to be indicated in patients with myasthenia gravis.

5. A normal labor at term, with a normal child, may be expected.

6. A few patients may not improve during the pregnant state, and possibly may become worse. With prostigmine treatment, however, such patients, in all cases which we observed, may be carried through to normal term.

DISCUSSION

DR. MARY A. B. BRAZIER: As far as our experience goes, those patients who were allowed to go to full term had normal deliveries, and we have no record of difficult labor. In fact, the labors were easy and short. There has been no evidence of transmission to the offspring.

DR. ROBERT S. SCHWAB: I should like to speak briefly of an experiment, a negative one, which E. B. Atwood and I carried out at the medical school. We thought myasthenia gravis might be due to a curare-like substance which was neutralized by pregnancy. We put rats in a bath of water and let them swim until they could swim no more. We found that white rats began to drown after twenty minutes. We injected a fixed amount of curare and found that we could reduce their period of activity before exhaustion to four minutes. We then made a group of rats pregnant to see whether pregnancy would protect them against the curare. All the rats, however, tired in four minutes. The results of the experiment were completely negative and showed that here pregnancy was no protection against curare, but, after all, we were dealing with white rats, not human beings, and with curare, not myasthenia gravis.

DR. AUGUSTUS S. ROSE: Dr. Viets pointed out that the patient voluntarily reduced the prostigmine intake during pregnancy. In view of the fact that prostigmine has a decided effect on the normal person, I should like to ask whether during pregnancy the tolerance to the prostigmine is reduced.

DR. HENRY R. VIETS: The question of tolerance to the drug, which Dr. Rose has raised, is indeed an interesting one. We have rarely found a patient who acquired such tolerance. When a patient has a remission during pregnancy I believe she feels at once the lack of need of the drug. The drug is so powerful and has such a remarkable response that the patient who no longer needs this response quickly discovers the fact. It is possible, moreover, that some of the untoward symptoms experienced by normal persons as the result of taking prostigmine bromide appear in the patient and give warning. To a normal person this drug is indeed a powerful stimulus. It is only the patient with myasthenia gravis who can take more than 1 or 2 tablets a day without a severe reaction. Patients with this disease, however, may take as many as 25 or more a day, and at least 1 patient has done so for two or three years. Occasionally, moreover,

patients take more than 2 tablets at one time, a few having taken 3, or even 4. Even on a high dosage over a long period, there appears to be no need to increase the amount of the drug in order to maintain a reasonable state of health, provided the patient is not having a relapse. An exception, however, must be made in the fatal cases, of which we have had a number in our series. Prostigmine in increased doses does not divert the catastrophe, and the patient dies of myasthenia in spite of the drug. Why this is so is still a mystery.

Many patients having a remission of the disease during their pregnancy are even in better than what is considered a normal state of health. One of our patients, a nurse, was able to do more work in her nursing home during her pregnancy than under ordinary circumstances. She could, for instance, carry two trays of food upstairs and beat up a dozen eggs without the slightest fatigue.

Attempts have been made to extract a substance from the amniotic fluid and from the placenta, without success. In view of the fact that remission sometimes takes place within the first month of pregnancy, before the placenta is well formed, one concludes that this organ is not the cause of the remission. One of our patients, for instance, began to take less prostigmine even before she missed her first period. It is evident, however, that some hormone or enzyme connected with pregnancy causes a marked effect on this disease. From what organ such a substance arises is at present unknown.

Book Reviews

Foundations for a Science of Personality. By Andras Angyal, M.D., Ph.D. Price $2.25. Pp. 398. New York: The Commonwealth Fund, 1941.

This book offers a serious effort at definition of the basic concepts underlying a holistic science of personality. The author has obviously been swayed in his thinking by a number of modern representatives of the holistic doctrine, including Smuts, Adolf Meyer, William Stern, A. Meyer (the biologist of Hamburg), von Uexküll and Bertalanffy, as well as by the *Gestalt* school. He defines the organism as a dynamic whole whose direction is toward an increase in autonomy in a setting in which the organism is under autonomous and heteronomous influences. The effort to increase autonomy appears to be a goal, not in the strict teleologic but in the directional sense. Under this general definition of biologic total processes the psychologic functions of symbolization, perception, imagination, thinking, emotion, conation, etc., are defined.

The biosphere is defined as the realm in which life takes place and is characterized by a system of tensions with bipolar organization: 1. From the standpoint of the organism these biospheric tensions reduce to drives, cravings and attitudes. 2. From the point of view of the object these tensions reduce to valences and demand qualities. Attitudes may be traced back to axioms of behavior, which have their psychologic counterpart in maxims of behavior, which in their systematic form comprise a philosophy of life. Object valences and demand qualities reduce to biologic relevancies. If the study of the biosphere is differentiated into an autonomous factor, or subject, and a heteronomous factor, or object, the sciences deriving from these two by parenthetic exclusion of one or more items may be summed up as follows:

Biosphere					
Subject (Organism)			Object (Environment)		
Parenthetic Exclusion	Subject Matter	Science	Parenthetic Exclusion	Subject Matter	Science
Symbolism	Somatic processes	Physiology	Symbolism	Physical properties	Physics; chemistry
Biospheric reference			Biospheric reference		
Somatic processes	Mental states and processes	Psychology	Physical properties	"Ideas"	Psychology
Biospheric reference			Biospheric reference		
Symbolism	Biospheric reference of somatic processes	Biology in the narrower sense of the word	Symbolism	Physical environment	Ecology? *Umweltslehre?*

The total organism does not exist in isolation, however, but lives in a social setting. To the latter factor the author does justice with the concept of the organismal trend toward homonomy, which is as compelling a bit of dynamism as is the trend toward increase of autonomy, and is opposed to the latter. Basic human trends take specific form both in the trend toward increased autonomy and in the trend toward homonomy. The author offers a tentative inventory of these items, all needing further study.

The problem of integration is conceded to be the most difficult topic of personality study. The author contrasts "relations" and "systems" and sees human integration as a system in which parts have significance only by virtue of their position in the system. The system may be formed of subsidiary systems, of variable fixity or plasticity. Integration occurs in three dimensions: depth, breadth and progression. Disturbances of integration in any one of these dimen-

sions bring about characteristic symptoms. For example, disturbance in integration in depth brings a separation between overt behavior and underlying dynamic items, resting in unawareness, in shallowness of performance, etc. Disturbance in breadth brings about dissociation. Disturbance in progression brings about frustration.

Angyal replaces the current concept of abnormality of behavior by a new term, bionegativity, defined as "a personality constellation in which one or more part processes disturb the total function of the organism."

In the final chapter the author views the course of life as a *Gestalt* organized in the dimension of time.

Enough has been said to indicate that this is a serious effort at the description and definition of concepts, basic for a study of personality from the holistic viewpoint. The material is abstract, but with actually few new terms, and the reader should not be alarmed. There is actually nothing in the book which cannot be easily grasped with the effort which it deserves. The presentation is somewhat ponderous. It could have been written in a lighter vein, avoiding a certain repetitiousness. This repetitiousness, however, appears not unnecessary in view of the very serious manner in which the material is couched. This is not something to read and lay aside, but something to study and attempt to grasp and apply to case material from both the normal and the pathologic sphere. The author's frequent reference to case material and to contemporary theories of psychopathology shows that he has made his own applications. (Perhaps the theories are imperative from the observations.) Neither is this just armchair philosophy of science, as holistic efforts have been accused of being. Basic concepts and their systematization appear to be necessary if one is to get further than the expression, illuminating in its day but somewhat trite by now, that psychiatry is a study of the personality as a whole. Calling attention to what is whole function and what is part function is a thankless but indispensable pedagogic task. Students may not like it; it may appear dull, but teachers at least must be able to think clearly on this matter if future research in psychiatry is to avoid the hazards inherent in the current slavish obeisance to fuzzy but catchy clichés with authoritarian sanction.

The author may be congratulated on having done an excellent piece of work, and every serious psychiatrist, teacher and research worker could profit by an effort to understand the basic concepts which are defined in this little book. The Commonwealth Fund has done a very presentable job with the actual bookmaking.

Self-Analysis. By Karen Horney. Price $3. Pp. 309. New York: W. W. Norton & Company, Inc., 1942

The title of this book, though accurate, is somewhat misleading. Although the author does give instructions to those who would analyze themselves, the actual experiences which she reports are derived from her patients, who have brought to her accounts of their progress during intervals of their analysis. Whether the suggestions she has derived from them could be of help to patients who are not in contact with an analyst is not clear.

Fortunately, the book does not depend on this point for its value. It deals largely with the interpretation of a few well chosen cases. The method of presentation is excellent, and is especially to be commended for its lack of jargon. The essential steps in the evolution and comprehension of each case are explained in nontechnical terms, easily comprehensible to any intelligent layman and restful to the nonanalytic physician. It should promote a wide understanding and tolerance of analytic methods.

Unfortunately, on the other hand, certain historic aspects of psychoanalytic theory are presented in a manner suggestive of bias. For example, Dr. Horney seems to interpret Freud's expectation that relief of inhibitions would release his patient's natural creative ability as an indifference to ideals, and to contrast it unfavorably with the ideals she would set. Luckily, such technical details are unlikely to mar the value of the book for those to whom it will mean the most. Many psychotherapeutists will find this a useful book to recommend to their patients.

INDEX TO VOLUME 47

The asterisk (*) preceding the page number indicates an original article in the Archives. Subject entries are made for all articles. Author entries are made for original articles and society transactions. Book Reviews, Obituaries and Society Transactions are indexed under these headings in their alphabetical order under the letters B, O and S, respectively.

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CONTENTS